

ORGANIZATION WITHIN THE PHARMACEUTICAL INDUSTRY
- A SURVEY

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ABSTRACT

A survey has been made of 12 U.S. and 5 U.K. companies in order to establish if there are any favored organizational structures in terms of pilot plant and related operations, production trouble shooting, clinical supplies manufacture and general engineering support services. Broad patterns of behavior become apparent in terms of the manner in which companies organize themselves to perform these functions. Communication, background and training of personnel and well-drawn lines of responsibility emerge as important factors in the efficient operation of the organizations surveyed.

This survey was undertaken in order to establish if there are any favored organizational structures in terms of pilot plant and related operations, production trouble shooting, clinical supplies manufacture, and general engineering support services. Senior Research and Development and Manufacturing personnel in 12 U.S. and 5 U.K. companies were contacted individually and asked to participate. The confidentiality of the survey was stressed and the questionnaire was designed to preserve anonymity. Without exception, everyone who was contacted agreed to complete the questionnaire. In actuality, while responses were received from all 17 companies, only 28 of the 34 individuals to whom questionnaires were sent eventually completed and returned the survey. In the U.S. 11 responses came from R&D - mainly Directors of Product Development. Ten replies were received from their counterparts in Production. Four of the 7 U.K. responses were from Directors or Heads of Pharmacy R&D, 2 were from Directors of Manufacturing and 1 was a joint submission from both areas.

Based on the estimated annual dollar sales in the U.S. or the U.K., the companies were classified as "small" (\$0-100 million), "medium" (\$100-300 million) or "large" (over \$300 million). Companies were also asked to describe themselves as either "ethical" or "diversified." The backgrounds of the 17 companies are summarized in Table 1.

Table 1. Companies surveyed

<u>Size of company</u>	<u>Location</u>	<u>Type of company</u>	
		<u>ethical</u>	<u>diversified</u>
Small - \$0-100 million	U.S.	4	0
	U.K.	0	0
Medium - \$100-300 million	U.S.	0	4
	U.K.	2	1
Large - over \$300 million	U.S.	3	1
	U.K.	2	0

The results of the survey are now discussed under the several headings used in the questionnaire sent to participants.

A. Scale up, pilot plant and pre-manufacturing process development

Within 11 of 12 of the U.S. companies and 4 of 5 in the U.K., Product Development has the major responsibility for these activities. In only one small ethical company in the U.S. and the medium diversified U.K. company were these activities organized within Manufacturing. One of the medium sized ethical U.K. companies noted that responsibility formally moved from Product Development to Manufacturing when the size of the pilot batch reached 50 Kg. One of the large U.K. companies reported the use of a "project team" approach, more common in the research side of R&D organizations, that involved Product Development, Production, and Engineering. Logically, all the Product Development groups reported within the R&D organization. Twelve of the 17 companies had separate* pilot plant facilities; of the remaining 5, 2 commented that they were contemplating the addition of such a facility.

The number of people involved in scale up, pilot plant and pre-manufacturing process development ranged from as low as 2 to as many as 51. However, it would appear that the higher numbers quoted arise from Product Development groups where no special group or individuals are formally assigned totally to pilot plant work. Presumably, here the formulator carries the formulation through from the development stage to scale up and into the pilot plant. Even though 12 of 17 companies reported separate pilot plant facilities, most of these (10 of 17) do not appear to have a separate group to man it. Of the remainder, 4 of 17 have separate groups (3 of which report to

* Not necessarily a separate building; could include a laboratory within Product Development set aside for these activities.

Product Development and the 4th to Production) while the remaining company expects to set up a separate group reporting to Production.

Most companies (13 of 17) are satisfied with their current arrangements, although this is not to say that there are no disadvantages. The major frustrations were contained in the responses received from Production personnel - understandable with 15 of the 17 groups reporting to R&D via Product Development. Not surprisingly, the 2 Product Development respondees from companies where scale up and pilot plant were a Production responsibility favored the transfer of these operations to Product Development.

The most frequently cited disadvantages from Production personnel were (a) inadequate communication with and/or appreciation of Production, particularly in terms of their need for a simple "robust" formulation capable of running successfully on existing equipment, (b) the lack of significant professional interaction between Product Development and Production groups, (c) often no clear transition point when a new product-to-be formally becomes the responsibility of Production, and (d) a poor appreciation by Product Development of the priorities and scheduling needs of Production. However, not one individual from Product Development currently responsible for these operations wished to relinquish control. The most frequently quoted advantage for Product Development to have responsibility for these activities was the opportunity, being free from production schedules, to spend more time "researching" the scale up. Product Development respondees obviously feel they have the capability of finding out why something works rather than simply establishing that it does work.

The educational background of those involved in scale up and pilot plant operations is varied. The majority have come through Product Development with, on average, 3 out of every 4 people being from

an R&D background rather than Production. With the larger companies, 5-8% of personnel were degreed engineers, although this appeared to be fortuitous rather than because of any deliberate policy to create an engineering subgroup. In the U.S., the larger the company the greater the percentage of PhDs employed in this activity, averaging 10, 16 and 22% in small, medium and large companies, respectively. In the U.K., PhDs in the medium and large companies surveyed were 5 and 25%, respectively. The breakdown is summarized in Table 2. Several conclusions can be drawn from this portion of the survey. Thus (a) Pilot plant operations apparently fit best with the Product Development group. (b) It is probably unnecessary to identify a separate group to conduct pilot plant work, although this will depend on the size of the Product Development group, the available expertise within the group, and the number and complexity of new products under development. Such factors as a relatively inexperienced Product Development group or numerous start-up operations overseas could make it desirable to form such a group. (c) Production personnel should be made aware of new products undergoing development and should be asked to comment on formulations at an early stage of development. At the same time, Product Development personnel must become well acquainted with Production's capabilities,

Table 2. Personnel in scale up, pilot plant and pre-manufacturing process development

Size of company	Location	Distribution of personnel (%)			
		non degreed	BS/MS	PhD	R&D background
Small	U.S.	40	50	10	67
	U.K.	--	--	--	--
Medium	U.S.	40	44	16	81
	U.K.	51	44	5	40
Large	U.S.	31	47	22	60
	U.K.	40	35	25	75

equipment and capacity. Short term secondments and/or exchanges of personnel should be considered as a means of strengthening communication and long term collaboration. (d) A formal procedure to alert Production that a developing product is going into a pilot plant stage is highly desirable, as is a clear point for "handing over" a product to Production. Several schemes exist within the companies surveyed. One, used by several respondees, is as follows: the first production run is supervised by Product Development (the pilot plant group if such exists), observed by the Production group responsible for technical support, and actually carried out by the Production staff. The second batch is supervised by Production's technical support group, observed by Product Development, and again manufactured by Production personnel. Finally, the third batch is handled by Production with both Product Development and Production's technical support group as observers. If satisfactory, the product is then formally transferred to Production. A few companies give Production the option to accept or reject a formulation offered to it by Product Development. This should at least ensure that Product Development starts talking to Production at an early stage in development! In all instances, transfer involves agreement on a product monograph that accompanies the product into Production.

B. Production trouble shooting and product support services

The majority (12 of 17) of companies are organized so that Production has the responsibility for this set of activities. In the other 5 cases, Product Development holds this responsibility while reporting to R&D. This latter arrangement does not appear to be dictated by the size or type of company, since these are varied (see Table 3). The number of personnel used in these activities ranged from 2 to 40; the larger the organization, the greater the number of people involved. On average, small companies used 5, medium companies 8, and large companies used 24 people. In most instances, the people staffing these activities had Production backgrounds. In the U.S. companies the bulk of the staff hold a BS degree, with the

Table 3. Personnel in production trouble shooting and product support service

<u>Size of company</u>	<u>Location</u>	<u>Distribution of personnel (%)</u>			
		<u>non degreed</u>	<u>BS/MS</u>	<u>PhD</u>	<u>Production background</u>
Small	U.S.	17	78	5	58
	U.K.	--	--	--	--
Medium	U.S.	7	86	7	69
	U.K.	50	50	0	88
Large	U.S.	26	59	15	44
	U.K.	52	35	13	23

percentage of PhDs increasing with the size of the company, a trend observed with other parts of the survey. In all U.S. companies, non-degreed personnel were in a minority, ranging from 7 to 26% of the total group. A higher percentage of non-degreed personnel were employed in U.K. companies. The average figures are presented in Table 3.

Overall, there was a strong feeling from the respondents that trouble shooting should be a Production responsibility. Convincing arguments put forward included the fact that the appropriate group is always present in the production facility; that a manufacturing oriented group is operating in a manufacturing setting; and that technical service personnel, coming from a manufacturing background, have good intrinsic communication with Production personnel. It was also felt that such an organization results in a group capable of giving a high priority to Production needs - an important consideration in an area where an appreciation of sales and financial accountability is felt to exist more than in Product Development.

In the minority of cases (5 of 17) where trouble shooting is a Product Development responsibility, the rationale advanced for such an arrangement was that it served to prevent an extemporaneous, expedient approach to problems, since Product Development is free from Production-type pressures. While a valid point, it seems likely from the responses received that most Production people would argue in favor of expediency, claiming that Product Development should have developed an adequately robust product, capable of being manufactured under Production conditions, in the first place.

Disadvantages noted by respondents related to the frequent absence of strong analytical support in the Production setting, particularly if some element of "research" was needed in the solution of a problem. This can result in frequent demands for help from Product Development who can end up feeling "put upon." Rather than hand the trouble shooting responsibility over to Product Development, it would seem more logical to improve the technical competence and background of the trouble shooting group. Only one individual advocated a change in organization, suggesting that the responsibility be transferred to a pilot plant group that is free of developmental functions.

It seems that the optimum arrangement is for the trouble shooting responsibility to be within Production and be handled by a strong group whose experience comes both from Production and Product Development. Some element of rotation from Production and Product Development into such a group would be useful in order to improve communication and expertise. There is little doubt that the trouble shooting group should have access to a high level of analytical support.

C. Clinical supplies manufacture

The manufacture of clinical supplies is seen as a logical activity of R&D, with 16 of 17 companies surveyed being so organized.

Predictably, the number of people assigned to this activity increases with the size of the organization as measured by sales volume, the average being 5, 9 and 13 in small, medium and large U.S. companies, respectively. The percentage of PhD and degreed personnel tend to increase with company size, as indicated in Table 4. Generally, the individual in charge of this operation has a Group Leader or Section Head title.

Several respondees reasonably claimed that such an organization allows the appropriate group (R&D) to set the priorities on what is still a research-intensive product. At the same time, good communications should exist between Product Development and the rest of R&D in order to facilitate preparation and modification (such as variations in dosage levels) when needed. Sixteen of 17 companies used Product Development (including pilot plant) equipment, plus Production facilities when necessary or appropriate. In one company responding, Product Development takes the product for clinical trial up to and including Phase III studies. If and when the project moves into Phase IV, Production takes over and manufactures the clinical supplies product. Some of the smaller companies do not have separate

Table 4. Personnel in clinical supplies manufacture

<u>Size of company</u>	<u>Location</u>	<u>Distribution of personnel (%)</u>			
		<u>non degreed</u>	<u>BS/MS</u>	<u>PhD</u>	<u>R&D background</u>
Small	U.S.	42	58	0	72
	U.K.	--	--	--	--
Medium	U.S.	58	29	13	78
	U.K.	62	31	7	38
Large	U.S.	26	58	16	81
	U.K.	70	22	8	100

clinical supplies manufacturing groups - presumably because the level of activity is too low to justify setting up a group devoted to this activity.

Disadvantages mentioned as a result of having clinical supplies manufacturing in Product Development included the difficulty in complying with GMPs in a developmental setting and the fact that priorities, from a Production point of view, may be set incorrectly. However, overall, the system in existence appears to work well and there was no real sentiment for change from either Product Development or Production.

While 16 of 17 companies place the responsibility for production of clinical supplies with Product Development, a lesser number (11 of 17) also charge this group with the responsibility for the release of these same products. Interestingly, the other 6 place this task with the Quality Assurance group or the Q.C. unit in Production. This appears to be a worthwhile arrangement that should provide for an independent and useful check on the product's specifications prior to its release into a clinical trial situation.

D. Engineering support services

Degreed engineers in both R&D and Q.C. are in a distinct minority; only 4 of 17 companies have such personnel. In contrast, 16 of the 17 have some form of centralized or corporate engineering group. However, it appears that not all such groups become involved in a meaningful way with the engineering problems associated with formulation development and production.

Seventeen of the 28 respondents commented on the need for engineers in pilot plant and process development. The great majority of these felt that there was need - particularly for process engineers. Several respondents made the point that if the only source of engineering talent is a corporate engineering group, then these engineers should be rotated out into the areas and divisions they were there to service.

At the same time, selected pharmacists could be seconded to the corporate engineering group. Ideally, if the size of the Product Development group justifies it, engineers should be permanently located in the pilot plant and process development operations.

E. Conclusions

It must be said that there are no real surprises coming out of this survey, which seems to be the first of its kind. The division of responsibilities within a company in the several areas examined are logical and appear to work well. Any group having a particular area of responsibility seems reluctant to relinquish that responsibility to another group or area. Communication between individual managers and their staffs in Product Development and Production comes through as a major advantage if functioning well - and a tremendous disadvantage if functioning poorly. It is obvious that both groups need to know each other's roles much better and seek to work in an atmosphere of collaboration and understanding. The transfer of responsibility between areas must be well defined and accepted by both groups. This lack of communication and knowledge of each groups function and area of responsibility was evident in some of the responses where conflicting data and points of view about the same portion of the survey were presented. Accurate job descriptions would help in this regard. Exchange of staff, even for short periods of time, would be beneficial even though potentially disruptive to work patterns and efficiency in the beginning. The long term benefits of such exchanges and secondments have to be significant.

Caution should be exercised in drawing too many conclusions from the tabulated data on the numbers and per cent distribution of personnel. The sample size was small, the variations between companies often high, the questions occasionally ambiguous and the responses not always equivocal.

This survey started out as an investigation of the organizational structure of pharmaceutical companies. This is an important aspect of the development and manufacture of new and existing drug entities. Several broad patterns of behavior have emerged. What has also emerged is that probably the most important aspect of all is the quality of people involved and they manner in which they interact and communicate. As one respondee commented, "variations in organization will work well if the personnel want it to work and communicate --- if the people are poor, no organization will correct that."