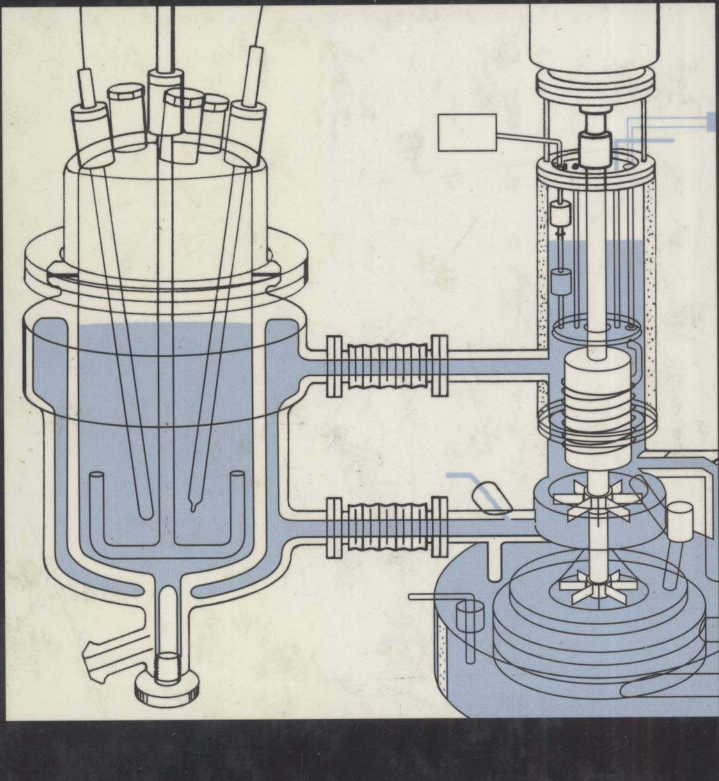
PILOT PLANTS AND SCALE-UP OF CHEMICAL PROCESSES



Edited by W. Hoyle

Pilot Plants and Scale-up of Chemical Processes

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Preface

Today, those involved in translating bench chemistry up to 10 - 100 litre pilot plants, and those operating such pilot plants, are continually being faced with new challenges. These challenges start at the development and design stage and involve the early collaboration of chemist and chemical engineer. This is particularly true when consideration is being given to batch versus continuous processing, and, for instance, in control and automation of batch processes. The first three papers cover these topics.

Maintaining and improving quality and standards, increasing yields and throughput, and ensuring safety are prime interests of pilot plant managers. Three papers present highly relevant authors' experiences in good manufacturing practice (GMP), statistical methods, and heat flow calorimetry and thermal analysis applied to pilot plants.

The last two papers cover very different but specific techniques. One outlines the development of processes for heavy metal removal from process effluent in the textile dyestuffs industry. The final paper discusses the interesting challenge of scaling up reactions carried out at temperatures down to -100 °C and their successful implementation to produce pharmaceutical intermediates.

The papers in this book are intended to present overviews or examples of best current practices in selected areas, including both chemists' and chemical engineers' perspectives. I am very grateful to all the contributors for giving so generously of their valuable time to make it possible to produce this book.

Bill Hoyle

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Design and Control

THE ROLE OF CHEMICAL ENGINEERS IN THE DESIGN AND OPERATION OF PILOT PLANTS

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1 INTRODUCTION

The development of effective chemical processes requires the integration of the skills, knowledge and experience of Chemists and Chemical Engineers. These two groups of professionals see the development process from different perspectives and have different objectives to satisfy. To appreciate their roles needs a clear understanding of what each can bring to the development process.

This is as relevant to the Pilot Plant stage or stages as it is to other steps in the development. Each group has expertise to bring to the design and operation of the Pilot Plant and is seeking specific information from the trials. Their contributions and expectations are also shaped by the purpose for undertaking the Pilot Plant trial.

This paper seeks to review the various purposes of Pilot Plant operations and to show in each context the benefits which can be obtained by the application of Chemical Engineering expertise and the enhanced benefits which can be achieved by gaining an understanding of the implications of the results for the design of the ultimate production plant and future bench scale experiments.

2 ROLES OF CHEMISTS AND ENGINEERS

To understand the contributions which are feasible and desirable from the two main parties in a process development programme, it is necessary to have an understanding of their individual knowledge bases, perspectives and interests. Put simply, the contribution of the Chemist is to identify the various combinations of chemicals, catalysts and conditions which will lead to optimal conversions to the desired product or products. The engineer's contribution is to identify practical, economic and safe equipment configurations which will allow these circumstances to be achieved.

Whilst the chemistry is unlikely to change as the scale of operation is increased, the same can not be said for the engineering. As will be discussed below, the ability to create specified conditions is a function of scale and there are likely to be subtle differences as the process is scaled up. An understanding of these and the implications in terms of product quality requires an integrated approach where both chemical and engineering principles are given equal weight.

Some of these problems can be avoided by involving Chemical Engineers in the design of the laboratory scale process as decisions made at that stage can significantly influence the ultimate viability of the plant. Engineers understand the influence that the physical design of the equipment and its operating characteristics are likely to have on the chemical process. This will allow predictions to be made as to how the product will change as the process is scaled up. Appropriate integration of Chemistry and Chemical Engineering can help to predict and explain some of the performance changes which occur as the process moves from the laboratory to full scale plant via the pilot plant.

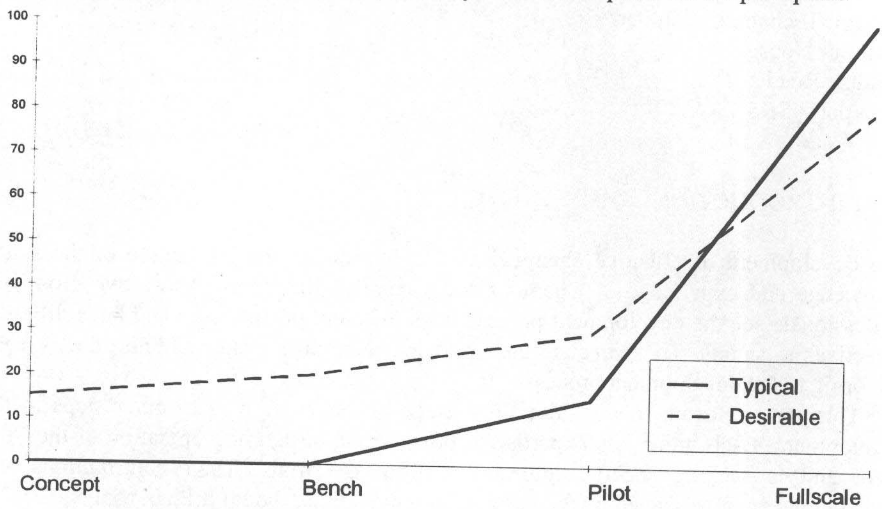

Figure 1 *Chemical engineering input to process development stages*

This will help minimise the risk of surprises. This is discussed in more detail below, but Figure 1 shows the normal contribution of the two disciplines at each stage of the development process together with recommendations of the levels which would be more conducive to effective process development. As will be seen, the basic recommendation is for a more co-operative approach where Chemical Engineers are involved earlier and the Chemists contribution continues into the design of the full scale plant. This should lead to both better plants and to improved process development cycles.

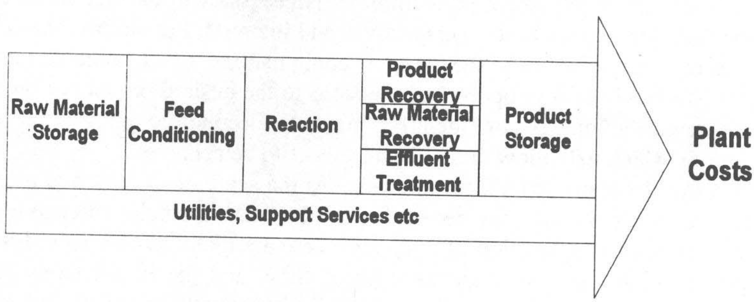

Figure 2 *Factors contributing to plant costs*

It is also important to realise that a successful process must operate in the real world, satisfying the constraints of Health and Safety, Environmental and Product Safety Regulations. This requires focus on the whole of the plant not just the reaction system. There is a danger that excessive optimisation of the reaction section will lead to difficulties in product isolation and purification, raw material recycling and solvent recovery areas. Figure 2 shows the elements which contribute to plant costs for a simple chemical process which illustrates the aspects of the overall plant which need to be considered and puts the reaction stage into perspective.

3 THE PURPOSES OF PILOT PLANTS

Pilot Plants are used at various stages of the Process Development cycle and fulfil different purposes depending on the needs at that time. The following are some of the purposes of Pilot Plants

- (a) To confirm bench scale chemistry on industrial style equipment
- (b) To prove that basic chemical know how works effectively
- (c) To provide information for subsequent scale-up
- (d) To provide design information for individual process items
- (e) To test the performance of proprietary equipment
- (f) To produce material for downstream processing or trials [Market or clinical]
- (g) To optimise plant performance
- (h) To investigate the production of new product grades or formulations

Whilst there are inputs which experienced Chemical Engineers can provide which are relevant to all of these cases, their contribution is highly dependant on the particular context. Advice on Safety, Environmental and Operability are relevant to each of the above situations. More specific advice or participation tailored to the particular situation will enhance the design of both the plant and the experimental programme and ensure that the maximum utility is obtained from the trials carried out. To examine these potential benefits, we need to focus on particular situations.

Depending on the particular situation, the most difficult design problems may reside in any of the development stages and the performance of the equipment at each stage may influence the results of the trials or their evaluation. It would be wrong to assume that valid inputs from Chemical Engineers were only relevant to the design of the final plant.

4 SCOPE FOR ENGINEERING CONTRIBUTION

4.1 Bench Scale Experimentation

The experiments carried out at the bench scale are very far removed from the conditions which will exist in an operating plant. In particular, the thermal history of the chemicals will be different in the two circumstances. This will influence the rate of reaction, distribution of products and formation of by-products. It is necessary to understand the mechanisms which lead to these changes so that the effects caused by the equipment and operating methods can be separated from the chemistry of the process. Only then can the process be scaled up effectively.

Similarly, choices made at this stage on the selection of solvents, operating temperatures and pressures and quality/yield or selectivity issues may have significant influences on the economics of the ultimate plant. It may be that decisions which have considerable effect may be made simply to ease the operation at the bench scale, because of availability or because of a lack of understanding of the implications. It is essential that such decisions are critically evaluated by people who are able to assess the implications at the plant scale.

As the experimentation proceeds it is important to bear in mind the implications of improving performance in one area if this leads to problems elsewhere. An example here would be the pursuit of increased selectivity towards the desired product which could result in the formation of a by-product which was less easy to separate. It is difficult to see how decisions on such matters can be made without taking a production perspective.

4.2 Pilot Plant

4.2.1 Process Confirmation. Generally, these applications are relatively easy to design, providing the basis of the laboratory trials is fully understood. There will frequently be difficulties with aspects such as the delivery of raw materials in controlled ways where a balance will need to be struck between what was effective in the laboratory and what will make sense on a full scale plant. In some cases, the design of the pilot plant may be more difficult than either that of the bench scale equipment or the final full scale plant, because the requirements do not match the capabilities of industrial equipment or the costs can not be justified.

Frequently in these cases, the process is adapted to meet the capabilities of an existing multipurpose pilot plant, consequently, there will be subtle differences between the pilot plant and the laboratory equipment. Whatever the circumstances, there will be differences which arise out of the increase in size of operation, changes in the types of equipment and possibly materials of construction.

One of the most significant problems in scaling up plant is that the area to volume ratio decreases as the scale is increased. This means that as the development moves from laboratory through the pilot plant to the full scale plant, heating and cooling becomes more difficult unless the aspect ratio of the equipment is changed. This is rarely acceptable as it usually leads to other problems.

A related design issue is the method of applying heat. In the laboratory, electric heating using mantles is the most common method, whilst larger scale equipment will tend to use hot liquids or steam. The former provides a constant heat flux with the surface temperature changing to meet the circumstances, whilst the latter provides constant temperature driving forces with the heat flux varying. This means that both the wall temperatures and the thermal history of the reactants is different at each scale of operation. This results in the formation of different products and can explain some of the situations where researchers are surprised to find that an apparently successful process can not be translated to the pilot plant scale.

Similar effects can be noted with vacuum systems where it is easier to obtain lower pressures on smaller equipment. In situations where boiling or distillation is required, it should be noted that the depth of liquid becomes important. At high vacuum levels, the static head of liquid can be sufficient to prevent boiling, this in turn will reduce the rate of heat transfer and increase wall temperatures, possibly leading to unexpected by-products.

These and related topics should demonstrate the importance of involving Chemical Engineers in the design of pilot plants for these types of duties, however there are other roles which should be considered. One key role is to decide on which process parameters to measure and record during the trial. This is important because if there are any problems it will be necessary to determine whether attention needs to be focused on the design of the pilot plant or on the understanding of the process chemistry. This may mean that additional instrumentation is required to allow the performance of heat exchangers and other equipment to be assessed.

As the equipment is set up for the trial, it will be necessary to consider the safety and environmental aspects of the intended operation. Engineers' working roles equip them to assess the nature and extent of safety related maters and to select approaches which minimise risk. It may be desirable to carry out an Hazard and Operability [HAZOP] Study to formally record the analysis of potential hazards and the methods selected to minimise them. Alternatively, a less rigorous approach may be more appropriate in some circumstances.

In any event, it will be necessary to ensure that adequate provisions are made for the relief of vessels and the containment of the relieved material. If rapid depressurisation or the formation of significant proportions of gas is envisaged, then it may be necessary to design for handling two phase relief. This is much more complex to assess and potentially more dangerous, possibly resulting in the discharge of the entire reactor contents [the champagne bottle effect]. If this is the case the additional specialist laboratory work will be required to generate the thermochemical data required for the design calculations.

Similarly with environmental matters, it is important to consider the requirements of Integrated Pollution Control and to convince oneself that the proposed methods for handling discharges represent BATNEEC [Best Practical Technique Not Entailing Excessive Cost]. This approach should be adopted whether the pilot plant comes under the ambit of the Environmental Protection Act [1990] or not.

One further aspect which is worth noting is that the chemicals used in the pilot plant may be subtly different from the analytical grade materials used in the laboratory trials. This may affect the process or product quality but may also have safety or environmental consequences. The process's sensitivity to the specification of the feedstock should be investigated if possible.

It may prove useful to have an engineer present during the trials, not only to comment on methods of overcoming some of the problems raised above, but also to observe the operation. Some effects which are unlikely to be addressed by simple record keeping and analysis may provide important inputs to the design of a suitable full scale plant. These would include observations of foaming or frothing, whether the process was easily controlled and any transient effects. These aspects influence performance at the bench scale and pilot plant levels but are generally more difficult to deal with in the design of larger scale plant, particularly if their importance is not understood and therefore they go unreported.

4.2.2 Know-how Confirmation. Many of the points discussed in the sub-section above apply equally well to this use of pilot plants, but there is a need for a somewhat different approach. In attempting to prove the utility of Process Know-how, it is necessary to be able to isolate those differences between the laboratory and pilot plant operations which are due to the effects of the different scale, changes in feedstock or operating methods. The analysis of the results should then account for these differences to allow a reasonable assessment of whether the chemistry of the process remained valid after scaleup.

There may be a case for repeating this analysis for the next stage of scale-up so that an assessment can be made of the likely performance of the full scale plant. The potential user of the know how is more likely to be interested in how the process will operate in a commercial scale plant than either laboratory or pilot plant versions. To assess these effects for anything other than the simplest of processes needs some Engineering input. Where the process requires recycle loops or the recovery of unreacted raw materials, the need for engineering input becomes even more necessary, particularly as pilot plant trials are unlikely to be maintained for long enough to allow such recycles to reach steady state.

4.2.3 Information for Scale-up. In this case, the Process Engineer may well be the immediate customer and will certainly be interested in the design of the pilot plant. Once again, many of the potential contributions discussed above remain important, but in this case, the parameters which ought to be measured during the pilot plant trials will be of particular importance to the Process Engineer. He is likely to be less interested in how closely the pilot plant performance matches that which was observed in the laboratory or will be needed on the production plant, than in how well the individual items of equipment perform.

Co-operation between the Chemist and the Chemical Engineer is vital in this case as it is essential that the engineer understands the mechanisms of any reaction, the factors which influence yields and selectivity and the nature of any by-products. As was discussed above, the thermal history of the reaction mass is likely to change subtly as the processes is scaled up, these changes are predictable and provided that sufficient knowledge is available, it should be possible to calculate the changes to the design of equipment which are needed to counter-act them. To achieve this may require that additional laboratory experimentation, which the Chemist may see as unnecessary, is carried out. It is necessary for both the Chemist and the Engineer to understand the need for this additional work and how it will be applied to the scale-up process.

In speciality and fine organic processes in particular, there is likely to be a dearth of decent physical property and volatility data and it may be necessary to design the experimental programme to investigate the effects of different assumptions. This tends to apply more to distillation stages than reaction as non-ideal systems are commonplace, but vapour liquid equilibrium data is scarce.

One area which is likely to need some attention at this stage is the amount, nature of and distribution of by-products. Laboratory data which are acceptable to Chemists to confirm their understanding of the process, are frequently totally inadequate for a Chemical Engineer to close a mass balance. There are frequently unknown species in product streams and laboratory mass balances are, for a variety of well understood reasons, rarely fully reconciled. Unfortunately, as the scale of the plant increases, the importance of both the unknown species and unexplained material losses becomes ever more important. A discrepancy of 5% in the mass balance of a 1 litre laboratory experiment is understandable and likely to be of little consequence, however when the plant is scaled up to tens of thousands of tonnes per year, it becomes very important. Even qualitative information from the laboratory trial which suggests where the discrepancies arose from can be very useful to the engineer. Material which escapes as a vapour needs to be addressed differently from residues which are burned onto the side of the flask. If the source of errors can be addressed from the laboratory trials, then it will be possible to make reasonable assumptions about how the process will perform on the pilot scale and on the basis of this make even better assumptions about how the full scale process will be affected. Once again, the most effective method of assessing this is for the Chemist and Engineer to work closely together as each has part of the knowledge and understanding needed.

4.2.4 Generation of Design Information for Individual Equipment Items The equipment required for certain unit operations is virtually impossible to design on a wholly theoretical basis and trials using a specially designed pilot plant are required to generate the necessary design data. A good example of this would be equipment for liquid:liquid mass transfer, or as more commonly known, solvent extraction.

This equipment needs to be scaled up by reference to a pilot plant designed to be geometrically similar to the intended full scale item. Assumptions need to be made about the type, size and shape of the device which it is intended to use on the full scale plant and this information is used to design a pilot plant which will model its operation. Ideally, the design will be sufficiently flexible to cover the range of probable outcomes, but there is a risk that several pilot plants will be needed to confirm the design of the full-scale plant.

The intent in designing the pilot plant is to provide dimensions which achieve identical flow patterns to those which will be observed in the plant scale equipment. The physics of flow mean that the scaling equations are rarely linear and that it is frequently impossible to model all aspects of the situation simultaneously. As with any design problem, compromise is needed.

To obtain reasonable equipment sizes, it is usually necessary to work with fairly small flows, this may present quite complex design problems as it is important to provide stable and steady flows. It is important also to be able to control the operation of the equipment over a fairly wide set of conditions. The number of parameters which need to be varied may then lead to a complex series of trials designed to allow the effects of each parameter to be isolated.

Additionally, the design may be constrained by requirements to observe qualitatively how the process is performing, and some of the information needed for design may depend heavily on witnessing changes in flow patterns. This may need glass viewing panels which may mean that the process can not be operated at the pressures which will be used on the full scale plant. It is important to understand how these changes will affect the operation of the unit and to allow for this in the design process. Similarly, the lack of availability of suitable equipment in the sizes needed for the pilot plant may severely restrict options on design and lead to less than satisfactory performance. In one development programme which the author was involved, this type of problem meant that the design of the pilot plant was much more complex than either that of the laboratory apparatus or the full scale plant.

When Pilot Plants are used for this type of investigation, they are almost exclusively engineering tools designed by engineers who will also direct their operation to ensure that the necessary results are obtained. The role of the chemist in this situation is to support the engineering activity with prompt and accurate analysis.

Another area which frequently needs attention in these situations, is to provide a means of generating the feedstocks to the unit being modelled and to treat any resultant streams. It may not be necessary or appropriate to provide a pilot plant for the remainder of the process which matches the flows needed for the one operation which is being modelled. This means that it may be necessary to design processes and or plants to service the section being piloted which will not be necessary on the full-scale plant. This again will require co-operation between the Chemist and the Engineer to ensure that the sensible minimum equipment is provided. It is not necessary that these conditioning and recovery plant are designed on the same basis as the section being modelled. It may be more appropriate to design solvent recovery units which are capable of handling all of the fluid generated on a trial as this may be more cost effective and easier to operate than to provide a distillation facility which matches the production flow from the pilot plant.

4.2.5 Testing Proprietary Equipment. This is frequently necessary for items such as filters, dryers and specialist heat transfer equipment. Many of the points made in the previous sub-section apply equally in this case. The contribution of the engineer is likely to be focused more closely on providing equipment to deliver the feed in a controlled manner in the necessary physical condition and to handle the streams which arise. The engineer will also be interested to ensure that the appropriate measurements and samples are taken to allow the performance of the equipment to be evaluated.

The contribution of the Chemist to these trials will depend entirely on the extent to which the performance of the unit influences the process.

4.2.6 Trial Production. To a large extent the relative contributions of each party in this case are identical to those in the sub-section 4.2.1 above. The likelihood is however that a number of trials will be undertaken and that there will be opportunities to vary operating conditions or using feedstocks from different sources. This will allow the possibility of some plant and process optimisation and the generation of more detailed information for design. In particular, running the process many times will give some indication of the variability of the process, identify those areas which require tighter control and highlight items of equipment where performance deteriorates over time. All of this information will provide very useful inputs to the subsequent design process.

In the event that the pilot plant does not produce the quantity or quality of product intended, the engineer should be involved in the troubleshooting exercise. This is because he will be able to assess the extent to which the equipment has contributed to the problems and should be able to suggest solutions. If the problems are more related to the chemistry of the process, it is likely that the solutions will change the operating conditions and the engineer will be needed to comment on the ability of the plant to cope with the revised operating regime.

4.2.7 Optimising Plant Performance. Frequently operating companies will maintain a pilot plant facility which can be operated in parallel with the full-scale plant. This allows trials to be carried out using different operating conditions, catalyst mixes or step durations. The main inputs to these plants are likely to be from the process chemists or production personnel. The comments made in the previous sub-section apply equally well here and consideration should be given to involving a Chemical Engineer in the optimisation programme, as this will enable the plant constraints to be included.

4.2.8 Recipe Development. From a practical viewpoint, this situation is virtually identical to that described in the previous sub-section. The scope for involving Process Engineers is the same.

4.3 Full Scale Plant Design

Normally, this stage is handled exclusively by engineers, and chemists are rarely involved. There are however benefits to be achieved by integrating the research and development chemists into the design team. This will ensure that their knowledge of the chemical mechanisms is taken into account.

The engineers involved in the design process must be aware of the areas of expertise of the Chemists so that effective consultation is encouraged. This can be seen as the reciprocal of the engineers input at earlier stages and will help to ensure that design compromises and decisions do not adversely affect the performance of the process.

5 CONCLUSIONS

Process development is a complex multi-discipline activity requiring theoretical knowledge, practical experience and perseverance. For it to be effective, it is essential that an holistic approach is adopted and that a balance is struck between often competing needs. This requires the integration of Chemists and Engineers. A linear approach where the input from Chemists precedes the input from Chemical Engineers will not ensure effective processes are developed.

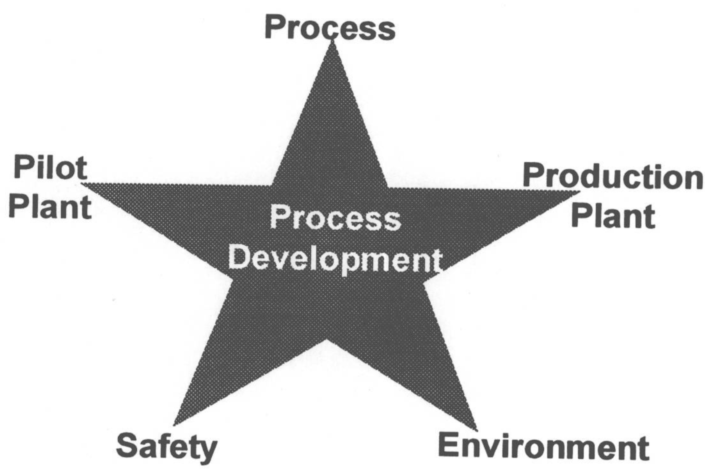

Figure 3 *Factors to be balanced in process development*

Figure 3 illustrates the most important elements to be addressed during the pilot plant stage of the process development cycle. Attention must be focused on all of these elements and the balance between them determined by the real needs of the development process. Chemists and Engineers each see the development process from different perspectives and have their own views of what is important. For successful development, they must however, be able to work as a team, which requires an understanding of and a respect for each group's potential contribution.

The quality of processes developed will be improved by involving Chemical Engineers earlier and the quality of the plants designed will benefit from the deeper understanding of the process that will result from involving Chemists in the design process. The synergy between the two disciplines must be harnessed by focusing attention on what each can contribute. This applies to all stages of the development cycle, not just the design and operation of pilot plants.

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