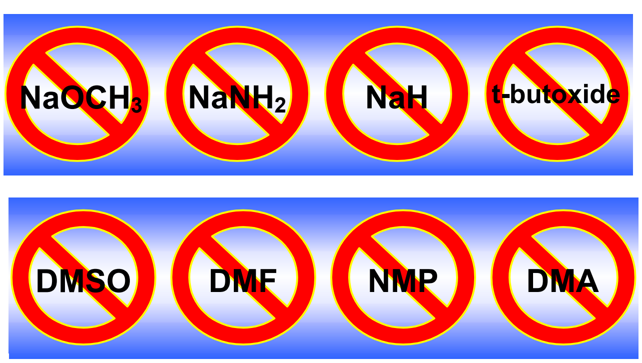
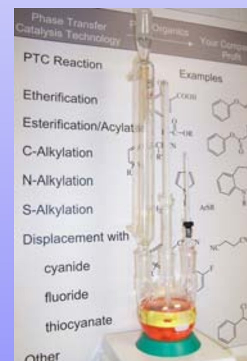
Phase-Transfer Catalysis Communications

Five Reasons Why Companies Miss PTC Process Improvement and Process Development Opportunities

by Marc Halpern
PTC Organics, Inc., 900 Briggs Road, Suite 145, Mt. Laurel, NJ 08054 USA
Tel: 856-222-1146, Fax: 856-222-1124, E-mail: mhalpern@ptcorganics.com

Every plant manager, process chemist, process engineer and plant operator "knows" that their onstream process is probably not fully optimized. Some processes are quite good and safely and consistently provide high quality product with high throughput and high plant operability. With other processes, you sometimes wonder how the process ever made it into production and why people have lived with it so long (sound familiar?)! Considering the process performance benefits of phase-transfer catalysis, "PTC" (e.g., very high productivity, acceptable or no solvent, high operability, etc.) it is surprising that many excellent PTC candidate processes do not use PTC. This article will describe the author's perception of the ***process of*** *process development and process improvement*, and how it specifically relates to the underutilization of PTC in industry. Understanding the real world barriers and solutions will help companies improve process performance by using PTC in new processes (development) and existing processes (retrofit).





Five Reasons For Missing PTC Process Improvement and Development

In order to understand why processes wind up the way they do, we should examine how process projects develop (see Figure on p. 36). The project begins when a compound is targeted for new development or when the performance of an existing process justifies the need for significant improvement. Once the decision is made to develop or improve a process, a series of events takes place, most of which are formal and some of which are barely done consciously. The reasons why companies miss PTC opportunities will be presented within the framework of the development process shown in the Figure. The reasons will be cited not necessarily in order of importance, they will be cited in the chronological order of process development.

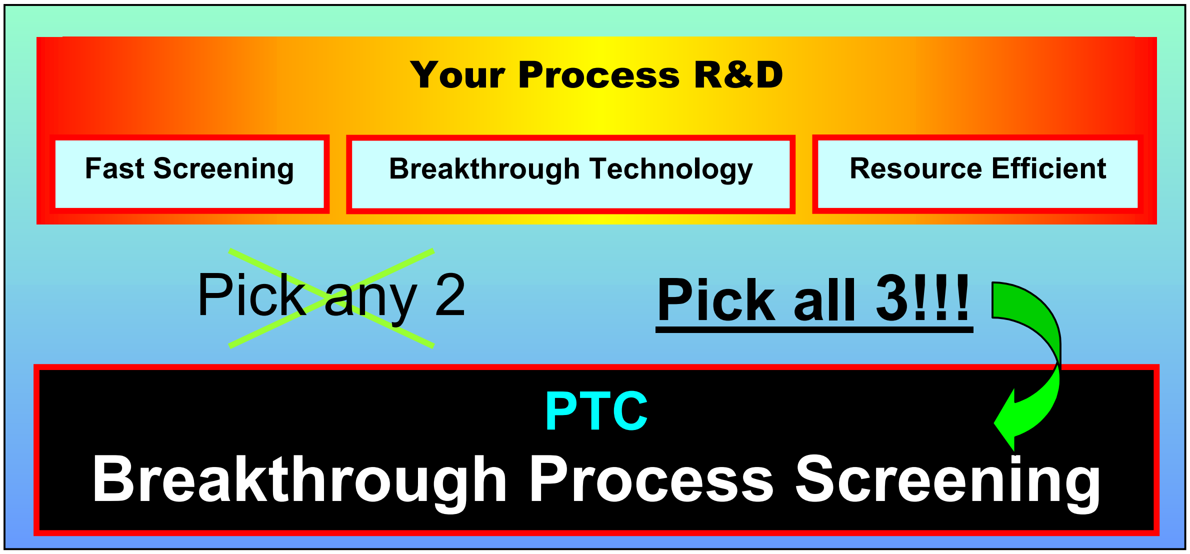
Chronological Reason #1: Didn't Think of PTC

The first two steps after the decision is made to develop or improve a process are divergent and convergent brainstorming. These steps can take a variety of forms. An integrated team of chemists and engineers may spend an entire day listing options for process improvement and up to a week for listing routes for new process development. Options may be suggested and duly noted without judgmental rejection of ideas, using a moderator and highly professional interactions (except that any participant may be allowed to throw a "nurf" ball at any participant who becomes judgmental during the divergent brainstorming stage). Ideas are not screened during this stage, they are only listed. In contrast to this formal process, not infrequently (especially for process improvement), a lone chemist may be assigned the process project. The lone chemist will review process options in his/her mind, sometimes for a few seconds, sometimes over several hours or sometimes intermittently during the course of a few days.

The actual process options and technologies brought up at a given divergent brainstorming session will depend on factors such as the participants' specific technical experience and personalities, corporate culture, time pressures and nature of the divergent brainstorming "session." Today, when PTC is an appropriate option, it is usually brought up during divergent brainstorming. However, if the process is, for example, 20 years old or just coming off patent, then PTC may not have been considered originally in the relatively early days of industrial PTC application. Even today, sometimes, chemists are not fully aware of the broad scope of PTC applications. For example, most chemists are aware that PTC is excellent for cyanation, esterification or C-/N-/O-/S-alkylation, but some chemists may not be aware of the advantageous application of PTC to dehydrohalogention, oxidation, carbonylation or hydrohalogenation. In these cases, "didn't think of PTC" is a valid barrier to ultimate commercialization. In addition, some corporate cultures encourage PTC, while others do not, just like some corporate cultures encourage Gringard reactions or using ethylene dichloride while others discourage these options. This will affect the listing of PTC as an option. Occasionally, a domineering personality present in a brainstorming session may induce reluctance in others toward suggesting less conventional options such as PTC (this defeats the purpose, but in reality happens anyway). Finally, divergent brainstorming sessions are often not conducted adequately because of time pressures, number of participants (e.g., one) or simply the perception that "a good chemist should know the one right answer immediately" (believe it or not, there are some who think that way!).

Chronological Reason #2: Didn't have the confidence that the PTC option would be developed within the deadline

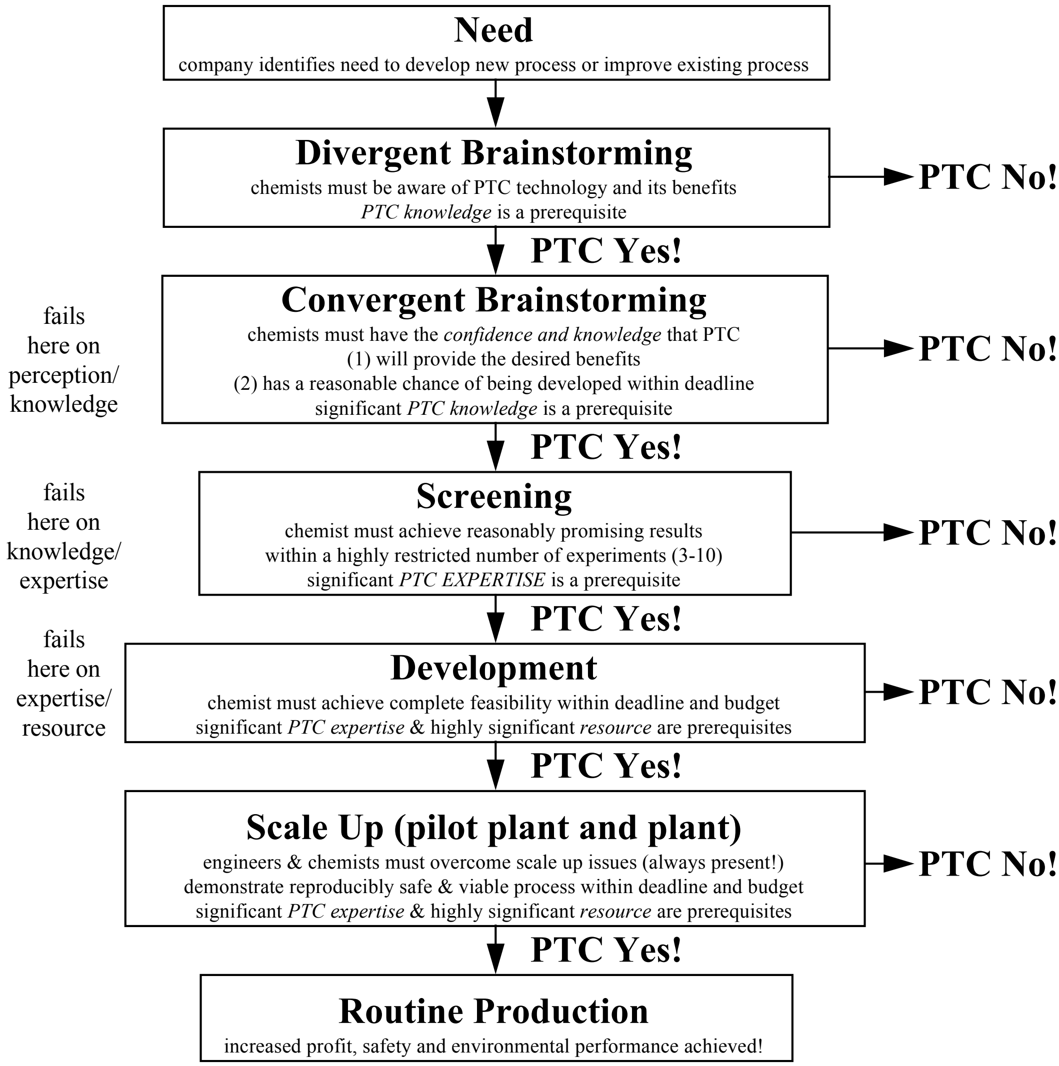
More PTC projects are inappropriately rejected during convergent brainstorming than in divergent brainstorming. During proper convergent brainstorming, the participants determine the criteria for screening the multitude of ideas suggested during divergent brainstorming. Typical criteria include yield, selectivity, reasonable cycle time, fit into existing equipment, additional unit operations, safety, health and environmental considerations, probability of success other costs and more. In order for PTC to survive convergent brainstorming, it is not enough for the chemist to be aware of the benefits and applications of PTC, the chemist must have the confidence that all issues can be adequately addressed within the project deadline. Depending on the level of experience with industrial PTC, the chemist may have concerns about choosing the proper catalyst and solvent, achieving the desired yield and cycle time, catalyst cost, catalyst separation from the product, catalyst stability, agitation and heat transfer in the two phase system and more. The



chemist is likely to confidently proceed with the PTC project if sufficient PTC expertise is available. There is a tradeoff between time and expertise. If the PTC expertise is not available, then the perception of the time required to resolve all of the practical issues may be to much to bear under the time and project management constraints.

The ***perception*** of prohibitive development time (justified or not) is often used to discount the PTC option during convergent brainstorming, especially when people just want to get on with a decision and start the project. A Research Director once told me: "We are cutting costs, we can't afford to look at PTC right now!" Since the premier measurable benefit of PTC is reducing cost of manufacture, the director was essentially expressing a ***lack of confidence*** in successful process improvement/development within resource constraints. The decision to embark on the PTC project before running the first experiment is a risk/benefit analysis. Depending on how departmental and individual performance is measured (and rewarded) the great benefit of PTC to the company (which may amount to $millions) may or may not outweigh the perceived risk and perceived uncertainty of project success. Thus, the actual profit opportunity or actual technical feasibility of the PTC option may be irrelevant to the extent that they are unknown to the decision makers.

An obvious way to deal with PTC technical uncertainty, as this stage, would be to consult with dedicated industrial PTC experts. PTC Organics provides free pre-screening of potential PTC process improvement opportunities and rapidly determines the probability of success. PTC Organics has broad industrial PTC experience (knowing what *hasn't* worked as well as what *has* worked) can bring great benefit if the PTC option is ultimately implemented. Sometimes overlooked, is the benefit that the industrial PTC experts bring by firmly concluding that the PTC project is *not* worth pursuing. A "negative" firm conclusion leads to reallocation of resources to options with more potential in a timely manner (time is money; in R&D, time is big opportunity-cost money).



Chronological Reason #3: Didn't obtain promising enough results within 3-10 experiments

After overcoming the awareness and psychological barriers to realizing the great potential benefit from PTC for a specific project, we reach the "screening" stage. Usually one to three (up to five) process options survive convergent brainstorming stage. The first experiments need to be performed to decide which single option will be pursued with intensity to commercialization. *The screening stage may be the stage at which more worthwhile PTC projects are lost.* This is the pinch point of the development process where expertise and constraints are most strained. Let's examine the issues.

Depending on the individual researcher's style, departmental culture and resource constraints, most preliminary screening studies must provide ***promising results within 3 to 10 experiments***. The results do not have to be optimal after 10 experiments (as low as three for impatient managers/researchers), but the results *must* be promising. If not, the project usually moves on to another surviving option or grudgingly reverts back to brainstorming. So the question becomes, can PTC be screened with promising results within a small number of experiments?

The answer is "yes" if the available research group has very significant PTC expertise and the answer is "doubtful" without this PTC expertise. At the outset of a PTC project, several choices have to be made, such as the identities and levels of catalyst, solvent, hydration and other parameters. As shown in earlier articles,[1,2,3] there are several pitfalls in choosing these parameters.

For example, the structural properties of the optimal catalysts for intrinsic reaction rate limited reactions are often totally opposite of those for transfer rate limited reactions. In other words, a commercially available catalyst which might work extremely well for certain PTC applications may be totally ineffective for other PTC applications. In fact, the use of tetrabutyl ammonium bromide, "TBAB" is sometimes (not always) an indication of a less than optimal process since it often gives mid-range reactivity. Sometimes, obtaining promising results is a strong function of the water present in the system in very narrow ranges. Some PTC reactions rates are significantly enhanced by nonpolar solvents, others by polar solvents. Some PTC reactions may be enhanced by co-catalysts. Thus, choosing "standard" PTC conditions may not give the desired results (especially if competing against other process options) and choosing non-standard PTC conditions may not yield promising results within 3-10 experiments. Given project deadlines and competing priorities, it is often the case that a superior PTC process option will be dropped if the standard PTC conditions are tried and "don't work."

Again, the obvious solution here is to supplement in-house PTC expertise with the dedicated PTC expertise of PTC Organics. PTC Organics has the highly specialized PTC expertise to navigate through the 14 interactive simultaneous process parameters required to achieve high performance and low cost.

In any case, if there is no alternative process and if R&D resources are not available for very extensive screening, the screening stage of a PTC project can be the most crucial to the success and continuation of the project.

Chronological Reason #4: The PTC process just wasn't feasible

Most projects (PTC or not) which pass the "screening" stage with promising results reach the "development" stage with a lot of work to do but with a lot of optimism. Usually, the process will be commercialized if the product itself is still viable. Most PTC projects which are unjustifiably dropped are usually done so before they reach this stage. Nevertheless, PTC projects can be dropped during the development stage for justified reasons and for non-justified reasons.

Once successful PTC screening is achieved, resource-efficient experimental programs can usually be designed and successfully executed to achieve high yield with desirable cycle time and solvent. This can be a barrier for difficult reactions or when PTC expertise is not readily available.

Probably the most difficult challenge to be met in the development stage of a PTC project is separation of catalyst from the product. Separation of phase-transfer catalyst from the product can be performed by extraction, distillation, recrystallization, adsorption or by using a polymer-bound phase-transfer catalyst. These catalyst separation methods require development time, but separation is an issue which clearly can be addressed with success. Catalyst separation is successfully and viably being performed for many hundreds of commercial PTC processes using commercially available phase-transfer catalysts. For example, many processes use TBAB, which is usually effectively separated by extraction. Occasionally, it is decided to drop a PTC project when the TBAB extraction/recovery unit operation is not as efficient as hoped. This is a shame since sometimes the TBAB process can be optimized by replacing this catalyst with a less expensive catalyst which is easier to separate and can induce higher reactivity. Without the added expertise relating to how to choose catalyst to simultaneously optimize reactivity and separation, companies sometimes conclude (justifiably in their eyes) that the PTC route is not feasible.

Sometimes, a process may require high temperature at which inexpensive phase-transfer catalysts may decompose. In such cases, the PTC application may be feasible using a more thermally stable phase-transfer catalyst. Chemists may be reluctant to try these catalysts because they are more expensive. A common mistake is

[1] Halpern, M. *Phase Trans. Catal. Comm.*, **1995**, *1*, 1
[2] Halpern, M. *Phase Trans. Catal. Comm.*, **1996**, *2*, 1
[3] Starks, C.; Liotta, C.; Halpern, M. *Phase-Transfer Catalysis: Fundamentals, Applications and Industrial Perspectives*, **1994**, Chapman and Hall, New York

to be concerned with the cost per kg of catalyst instead of the cost of the catalyst per kg of product.

Other scale up issues need to be addressed in PTC systems, most notably agitation and heat transfer, both of which are always scale up issues. Over-agitation can be a problem (promoting non-catalyzed interfacial side reactions) as well as under-agitation (lower reactivity due to under-agitation, which is more intuitive to engineers). Agitation can also be an issue in solid-liquid PTC systems. Other issues which may require development time may include catalyst decomposition (and impurities derived therefrom), solvent recovery and catalyst waste treatment (some quats are biocides which may upset a waste water treatment plant).

Any combination of the above reasons may truly render a PTC process option not feasible. On the other hand, the barriers may usually be overcome by applying more acquired expertise (why reinvent the wheel if highly specialized PTC experts may have the answer) or more development time. Those who say that development time is at a premium should remember that increased profit *is* a premium. The development investment must be weighed against the potential benefit. The PTC option either offers great profit and/or environmental advantage, or it doesn't! Decisions at all stages should be made according to the anticipated return on investment. Specifically, one must balance the development investment with the resulting process the plant managers and P&L executives will have to live with (or have been living with) for years to come.

Reason #5: Resistance to Change

Organizational resistance to change was covered in a previous article.[2] No matter how much convincing data can be provided for the PTC (or other) process improvement, organizational resistance to change can often wipe aside progress (e.g., "we lived with this process for 10 years...we'll live with it another 10 years, and besides, we can't risk any production down time or delay the launch of the new product just to try an improvement." Hopefully this doesn't happen at your company). The most powerful antidote to organizational resistance to change is change within the organization (e.g., promotion of a key manager). The second most potent antidote is an energetic charismatic champion armed with piles of firmly conclusive data and testimony to support the change. The guideline for combating organizational resistance to change is to evaluate what is best for the company (profit and environmental performance) and incorporate the conclusion during all stages of process improvement or development project.

In summary, PTC may be rejected as a process option during process improvement or development for a variety of justified or unjustified reasons. If the reasons are unjustified then once the non-PTC process is implemented, the company will "leave money on the table" and forgo performance until someone discovers and champions the justified PTC option.

The initial stages of evaluating options for process improvement/development affect the final outcome and process performance as much as or more than the later stages. This is because upon completing the initial stages of option evaluation, the options chosen are locked in for the longer development process. If project overload, technology bias or other factors prevail, key stages of initial option evaluation are compressed, restricted or even by-passed altogether. Ineffective initial evaluation of process options usually results in lower final process performance and longer development time, which are not likely to be recognized! Lost opportunities resulting from ineffective initial evaluation stages are common in organic chemical process improvement and development. The leading causes of missing opportunities using phase-transfer catalysis occur more often during the brainstorming and screening stages and sometimes during the prolonged development stage. Greater performance may be realized by (1) properly balancing development investment against potential benefit and (2) acquiring highly cost effective industrial PTC expertise as early in the process as possible.

About the Author

Dr. Marc E. Halpern is a leading authority on **increasing profit** using phase-transfer catalysis (PTC) technology. Dr. Halpern is the founder of PTC Organics, Inc. the only company dedicated exclusively to enhancing customer profit and process performance by developing high-performance low-cost processes for the manufacture of organic chemicals using Phase Transfer Catalysis. Dr. Halpern helped companies save > $150 million in process improvements and has provided PTC services at > 160 industrial sites in the US, Europe, the Middle East and Asia.

Dr. Halpern has authored or co-authored the classic books and training programs "*Phase-Transfer Catalysis: Fundamentals, Applications and Industrial Perspectives*" (Chapman & Hall, 1994) "*Phase-Transfer Catalysis: Mechanism and Syntheses*" (ACS Symposium Series #659, 1997), "*Practical Phase-Transfer Catalysis*" (320 chemists trained in the US, UK, Germany, Switzerland, Austria, Holland, Israel and Italy). Dr. Halpern founded PTC Communications, Inc., publisher of the journal "Phase-Transfer Catalysis Communications." PTC Communications, Inc. distributes this journal free of charge to industrial customers. Dr. Halpern innovated the guidelines for evaluation and optimization of new PTC applications and invented the accessibility parameter for characterizing the effect of phase-transfer catalyst structure on reactivity and selectivity. Dr. Halpern has an impressive track record as an Organic Process Chemist, a Supervisor of Process Chemistry Research and Director of Research and Development over a 19 year period in the chemical industry. Dr. Halpern currently dedicates his full time to phase-transfer catalysis.

Dr. Halpern would appreciate your comments and questions about this article and about industrial phase-transfer catalysis.

Phase-Transfer Catalysis Communications

Published by: PTC Communications, Inc.
900 Briggs Road, Suite 145
Mt. Laurel, NJ 08054 USA
Telephone (856) 222-1146
All correspondence and change of address should be sent to the address above.

Proper safety precautions must always be taken when performing chemical reactions, including phase-transfer catalysis reactions.