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'The Changing Face of Process Development & Chemical Manufacturing – A View from the Regulators on Continuous Manufacturing'

Abstract: Industry wide there is a drive for resource efficiency and flexibility, to adapt quickly in what is increasingly becoming a volatile, changing marketplace. As the 'patent cliff' looms for many high-volume API's, there is also a shift away from blockbusters towards lower volume, higher potency API's. This presents an opportunity to adopt newer methods of production that are more suited to the needs of flexible, lower volume, increased potency products, such as continuous manufacturing. Whilst an increasing number of continuous processes are being developed, one question continues to come up '*how do regulators feel about continuous manufacturing?*'. At a recent symposium, Dr Janet Woodcock Director of the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA) congratulated participants on the progress made over the past two years and confirmed that the '*FDA will not be a barrier*' for continuous manufacturing. This and other events show an industry in transition, herein we provide an overview of the current regulatory perspective on continuous manufacturing.



Figure 1. Example of a modular, multi-stage continuous flow plant [1-4].

Background: In recent weeks' we have heard Klavs Jensen [5] herald that 'Flow Chemistry – Microreaction Technology Comes of Age', Angeli Mehta [6] informing us of 'The Flow Revolution' and Carrie Cao [7] reporting on 'Flow Chemistry: Pathway for API Manufacturing'. There has undoubtedly been a noticeable shift in the acceptance of 'Flow Chemistry' within industry and academia, with questions changing from 'what can we use the technique for?', to 'do the regulators allow continuous manufacturing?' and 'how do we convince our regulatory colleagues, now we have technical proof?'.

These observations are supported by the findings of an industry-wide survey, summarised by Marks *et al.* [8], whereby 62 % of respondents involved in engineering or operations roles stated that regulatory challenges were their biggest concern when considering adoption of new technologies. With that said, an encouraging 44 % had employed continuous manufacturing as part of facility modernisation proposals.

In the past six months' there have been two noteworthy conferences that have focused on the regulatory aspects associated with the use of continuous manufacturing (or CM), firstly the 2nd International Symposium on Continuous Manufacturing of Pharmaceuticals (ISCMP) (September 26-27th 2016, Boston, USA) [9] and more recently CM2017 (February 22-23rd 2017, Dublin, Ireland) [10]. In May 2017, a regulatory whitepaper was issued as output from the 2nd ISCMP meeting for comment and will shortly be finalised [11]. Herein is given a personal account of the take home messages from these events and recent publications by the Food and Drug Administration (FDA), together with comments on how the technology is changing process development and manufacturing. For those of you that are new to the field, the whitepaper starts with an introduction to this emerging technology.

What is it & Why use Continuous Flow? Whilst bulk and petrochemical industries have benefited from the advantages of continuous flow manufacturing for decades, they have only recently been joined by fine chemical, speciality chemical and pharmaceutical manufacturers – this is leading to a change in the skills required in these sectors.

Chemical engineers are trained to think in terms of continuous processes, synthetic chemists more often think in batch; having received the same training over the decades and with basic hardware changing little over the centuries. Consequently, the routes that are developed by the bench chemist are often carried out under non-ideal conditions, with the goal being to obtain the compound as fast as possible. Little regard is given to the development of a synthetic route that is efficient and scalable just in case the compound needs to be prepared in larger quantities [12]. Looking at this in more detail, this can mean that to gain reaction control (be it thermal or selectivity), the chemist often chooses to use a large volume of solvent, employ deep cryogenic conditions, use long dosing times and selects stoichiometric reagents over catalytic ones.

Interestingly, chemists pay little attention to the mixing type or stirring speed and thermal efficiency of the regulation technique employed in a lab-scale batch experiment. In comparison, reaction kinetics coupled with heat and mass transfer are all parameters that the process chemist considers when looking to the viability of a process for scale-up. It is these differences in the way of working that can be one source of challenges that are later encountered on scale-up, if they could be considered at an earlier stage, time could be saved and the need for route re-development minimised. When looking to the toolbox available to the modern synthetic lab chemist, the conventional round-bottomed flask was last Century joined by the microwave synthesiser [13] and more recently continuous flow reactors; a review by Baumann and Baxendale [14] summarises the synthesis of numerous API's using continuous flow techniques. An article in Nature by Baker [15] also stresses the importance to development robust and repeatable experimental protocols.

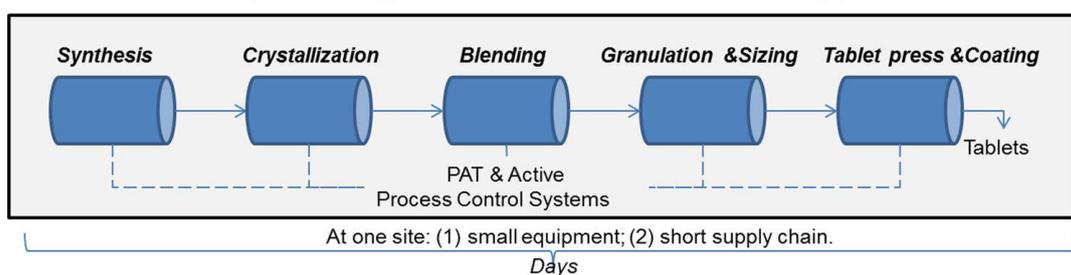
When compared to stirred vessels, materials are constantly dosed into a flow reactor and products are constantly removed (Table 1 & Figure 2) [16]. This means that flow reactors have significant processing advantages over batch which included improved thermal management, enhanced mixing control and access to larger operating windows (reaction time, temperature & pressure); as a result, safe, efficient, robust and sustainable production processes can be developed. Owing to their nature, continuous processes lend themselves well to strict control of process parameters *i.e.* reactant ratio (stoichiometry), reaction time, system temperature and pressure, facilitating Quality by Design (QbD) and improved process control/understanding *via* the use of Process Analytical Technology (PAT). Benefits are not only harnessed for the reaction steps, improved reaction control can also lead to reduced by-product formation and un-reacted starting materials – which can have the effect of simplifying the steps required for product isolation, potentially reducing operating costs.

Applicable at both the lab, pilot and production scale (Figure 3), continuous flow reactor technology can benefit both early stage researchers, process development chemists/engineers and plant managers through the development and implementation of good chemical manufacturing processes [17]. The technology also allows process intensification, which at its heart is focussed on the 'production of more with less' [18].

Batch Process	Continuous Process
<ul style="list-style-type: none"> Raw material(s) is charged into a system at the beginning of a process and the product is discharged all at once after a period of time. No ingredients cross the system boundaries from the time the raw material(s) is charged and the product is discharged. 	<ul style="list-style-type: none"> Raw material(s) and product(s) are continuously charged into the system, and discharged from the system respectively, throughout the duration of the process.

Table 1. A comparison of definitions for batch and flow processes.

A conceptual integrated continuous manufacturing process



A typical batch manufacturing process

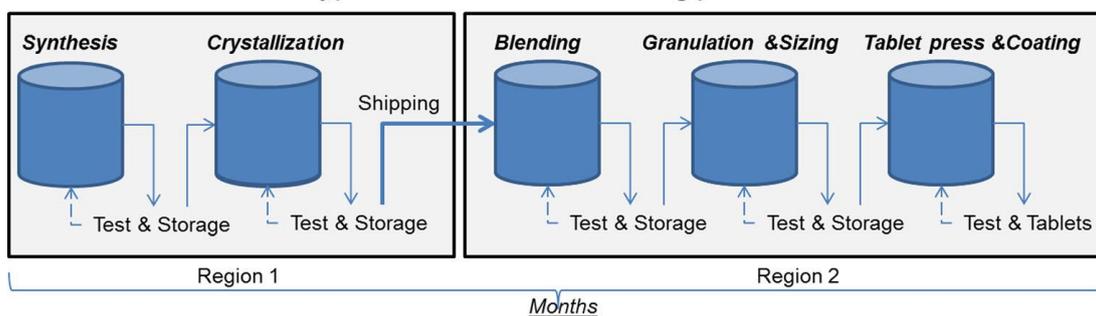


Figure 2. Schematic comparing an integrated continuous manufacturing process with a typical batch process [19].



Figure 3. A range of reactor products suited for research, development and production under continuous flow conditions.

How to Apply Continuous Process Technology? Flow reactors give experimentalists the option to use their equipment to gain the required process knowledge and reaction control along the scale-up path, rather than looking to change the chemistry, as has been historically the route taken – fitting new processes into existing batch infrastructure. Key to the successful implementation of continuous processing at an industrial scale is to gain a solid understanding of your process at an early stage *via* reaction kinetics, reaction calorimetry and a knowledge of physical properties (viscosity, density, specific heat capacity, solubility *etc.*).

Sharratt of ICES (Institute of Chemical and Engineering Sciences, Singapore) comments [20], as do many within the industry, that ‘approaches to the design of batch processes for high value chemicals are well understood’, so too ‘proven approaches exist for the design of (large) continuous chemical production processes’. The chemical industry is however now finding its way with the development of robust, rapid and cost effective methods for application of continuous flow to smaller scale, higher value specialty, fine chemical and pharmaceutical manufacturing.

When looking to the pharmaceutical industry specifically, the ability to design in quality is viewed as the most significant advantage of continuous manufacturing. Looking to the specifics of process optimisation, there is an on-going debate over the use of kinetic vs. statistical models when developing a process [21]. In a recent industrial case, Berry (GSK) *et al.* [22] clearly demonstrated significant time and cost savings by utilising kinetic modelling vs. Design of experiment (DoE). Performing 25 reactions in place of 80 (outlined by DoE), GSK reduced the quantity of API required for the work and the kinetic model aided with later process scale up activities.

Roberge *et al.* [23] describes a ‘notable shift in the development viewpoint within the industry to one where it is accepted that a continuous flow process does not have a longer development time or take more resources than batch’ – a view that is attributed to increased availability of standardised tools and more recently ‘plug & play’ process controls. These developments have facilitated the adoption of continuous flow in three key areas of process development;

1. Proof of concept
 - a. Assessment of solubility characteristics, response to temperature, pressure, stoichiometry *etc.*
2. Process optimisation
 - a. Maximising conversion, yield, selectivity, material efficiency
 - b. Identifying thermal demands of the process
3. Long term operation *i.e.* miniplant
 - a. Assessment of process robustness
 - b. Calculation of plant size to access target production volume and/or rate

With each step acting as a stage gate, determining go or no-go for the project, there is a clear path for implementation emerging within Companies.

Summary: Until recently it could be said that early adopters were mainly focussed on developing continuous flow techniques by taking existing products/batch protocols and transferring them to continuous flow equipment. When transforming a process from batch to continuous, it is important to identify where the process can be intensified *i.e.* what currently limits the process? and what are the critical parameters in terms of process safety and product quality?

We are however starting to see more and more processes developed from scratch, directly under continuous conditions, with a view of utilising the technique for small and large-scale manufacturing.

Based on User feedback, the benefits of continuous flow reaction technology are reported to include;

- Increased process safety
 - Low reactant hold-up
 - Excellent thermal & mass transfer
 - Reduced plant size
 - Reduced operator exposure
- Increased reaction control
 - Higher reaction selectivity – leading to increased yield, reduced raw material costs & downstream isolation
 - Reduced safety hazards
 - Improved process stability leading to increased consistency between campaigns
 - Potential financial savings through process intensification
- Shorter development times
 - Faster time to market – important for breakthrough therapies
 - Potential to reduce downstream isolation steps
 - Reduced development costs
- Improved economics
 - Reduced CAPEX – smaller, more productive equipment
 - Reduced OPEX – lower number of operators, less waste & rejects
 - Increased revenue from new products or larger market share
 - Shorter supply chains
- Societal benefits
 - Safer, cleaner manufacturing
 - Increased operator safety
 - Reduced risk of accidental release

As with any new technique, there is a learning curve associated with its use and implementation. With an increasing number of academic institutions training graduate and postgraduate students, researchers with at least a prior theoretical knowledge of the technique are now entering the industry. Whilst this can only help to accelerate the further adoption of continuous manufacturing, there is still a long way to go to bridge the skills gap that currently exists, particularly relating to practical experience. One important change within Companies that we have seen work well is to build multi-disciplinary Teams that bridge R&D, Process Development, Production and Quality/Regulatory departments. Having a common goal and involving all perspectives from the outset has been shown to accelerate progress when implementing new approaches within a Company.

Modernising Pharmaceutical Manufacturing: Whilst it is clear that significant scientific advances have been made both academically and industrially as the field of continuous manufacturing continues to grow, concerns have arisen as to the regulatory bodies views and acceptance of a change from 'batch manufacturing to flow'. The message from the FDA could not be clearer '*the FDA supports the implementation of continuous manufacturing using science and risk-based approaches*' [19].

Continuous processing has the potential to address several issues that are faced by pharmaceutical manufacturers such as a lack of agility, flexibility, robustness and production costs – points that form part of the vision associated with the FDA's 'Pharmaceutical Quality for the 21st Century Initiative' [24]. The ability to turndown, or conversely up, the production capacities of such continuous systems, followed by replication to increase production volumes, or change production site, makes continuous manufacturing appealing as a tool to minimise the impact of drugs shortages. When questioned on this, Lee [9] was supportive of modular plant replication and deployment in different territories as systems can be built off site, validated and delivered ready to hook-up to services.

The FDA also states that continuous manufacturing is well aligned with QbD initiatives, in which a systematic and science-based approach is taken towards pharmaceutical development to afford robust processes – taking away the reliance on testing for compliance [25]. By utilising continuous flow technology within the laboratory, enhanced product and process understanding can be gained ahead of implementing the techniques at a production scale. The employment of control strategies which maintain a process in a state of control can give rise to processes that are highly efficient, robust and cost effective – reducing significantly the costs associated with the generation of out of specification material [26].

Whilst bulk and petrochemical industries have benefited from the advantages of continuous flow manufacturing for decades, they have more recently been joined by contract manufacturers providing valuable, flexible resource support to the pharmaceutical industry. With techniques for minimising raw material consumption, increasing target selectivity and simplifying downstream unit operations all receiving attention as reasons for implementing the technique. Just this month, Omnicem (Belgium) announced the completion of a commercial scale manufacturing campaign using a mobile installation capable of up to 100 kg quantities [27].

Regulatory Viewpoint: In 2011, Woodcock predicted *'in the next 25 years current manufacturing processes are abandoned in favour of cleaner, flexible, more efficient continuous manufacturing'* [28] and more recently commented *'flow is an enabler'* that the FDA are supportive of. By improving the manufacture of pharmaceuticals there are the obvious societal benefits such as reduced treatment costs, fewer shortages but also a reduction in the required 'regulatory oversight', which has the potential to free up resources for use in higher risk areas. In 2014, Woodcock [29] re-emphasised the FDA's vision of an *'agile, flexible pharmaceutical manufacturing sector that reliably produces high quality drugs without extensive regulatory oversight'*. Kirschneck *et al.* [30] commented that the key to success for process development is to make the shift from iterative development to processes that are *'right first time'* – to achieve this requires knowledge of your process and the use of adequate process controls. Moore, acting Director of FDA's office New Drug Quality Assessment stated that continuous manufacturing has the potential to *'not only meet current expectations, but to really give enhanced product quality over what some of the current batch technology provides'*. Continuous manufacturing offers the potential to move away from large-scale, capital intensive production installations towards decentralised, small scale units that can be replicated and deployed at the most appropriate site. This mode of operation has potential to reduce the time to market for breakthrough therapies, where accelerated timelines can be a challenge when planning to scale-up in batch, and response to outbreaks.

In 2014, at the first ISCMP organised by CMAC and MIT, Badman and Trout opened the event by stating *'since the future of the industry is continuous manufacturing, the time to start realising the vision, and thus reaping the benefits, is now'* [29]. This event centred on the fact that industry wide there is a drive for resource efficiency, in response to rising energy costs, and flexibility in terms of being ready to adapt in what is increasingly becoming a volatile, changing marketplace. As the shift in the pharmaceutical industry away from blockbusters and towards lower volume, higher potency API's continues, there is a mis-match with existing infrastructure in terms of capacity. This gives an opportunity to adopt newer methods of manufacture that are more suited to the needs of flexible, lower volume production.

In 2016, Trout opened the 2nd ISCMP by stating tremendous progress had been made since the 1st ISCMP [6]. To date there are scant examples of end to end manufacturing (refers to both drug substance and drug product being continuous and integrated) outside academia, however there is significant progress made with Companies favouring hybrid approaches that employ a combination of batch and continuous steps. At the same event, Woodcock [6] stated how encouraged she was to see the theory of two years ago becoming *'we are doing this'* and saying that the industry *'has reached a tipping point'*. Emphasis was put on acknowledging that *'manufacturing should be viewed as a competency'* and *'manufacturing should not be choke point for new therapies'*. In her wrap-up, she summarised *'advanced techniques provide an opportunity for high quality, reliable precision medicines'* and an *'agile pharmaceutical sector is needed so that it can better serve patients and respond to crises'*.

This was later emphasised by her colleague Capacci-Daniel [31] who urged the industry to *'build quality into the process design'* and use the technology to result in 'faster delivery to patients' confirming that the 'use of continuous manufacturing is highly compatible with cGMP's'.

Not Just the FDA! As pharmaceutical manufacturing is a global enterprise, there is a need to cooperate across regulatory agencies. This is why it is gratifying to see that it is not just the FDA who are speaking out on the use of continuous manufacturing, the European Medicines Agency (EMA) are well aligned with the FDA and at the CM2017 symposium, Norton [32] referred to the current experience within Medicines and Healthcare Products Regulatory Agency (MHRA) of inspecting CM facilities. At ISCMP 2016, Matsuda of the Pharmaceuticals and Medical Devices Agency (PDMA, Japan) informed that they were planning to set up an emerging technologies team through which they could collaborate with regulatory bodies and industry called Innovative Manufacturing Technology Working Group [33].

So, with a clear statement of support from the regulators, what has led to hesitation within Companies?

What is a 'Batch'? The most frequent question that we receive here at Chemtrix from regulatory departments is 'how do we define a batch produced in a flow reactor?' In recent meetings, the FDA has said *'define it in any way that you want as long as you're consistent with the definition and you define it up front.'*

Current cGMP regulations [34] describe a 'batch' as a specific quantity of drug or other material that is intended to have uniform character and quality within specified limits and is produced according to a single manufacturing order during the same cycle of manufacture. Nothing in the aforementioned statement relates to the method of manufacture, be it a batch tank or a flow reactor, it simply refers to the amount of material produced. Traceability of material used within a process is key, when considering the potential need of recalls *etc.*, therefore it is essential to consider material traceability in your definition of a batch.

When considering how you want to define a batch of material produced utilising continuous manufacturing, there are several approaches that can be used. For example, you can define by;

1. Volume (XX litres)
2. Time period (XX hours)
3. Input batch processed

Most importantly, you must carefully align the control strategy to ensure uniform quality exists within the batch.

Control Strategy: The purpose of the control strategy is to ensure that the product quality remains compliant with the defined and accepted quality criteria for the duration of operation. There are three levels of control strategy that can be applied;

Level 1 – Is based on an active process control system to maintain quality attributes.

This approach allows automatic adjustment of process parameters in response to disturbances or changes to ensure that the quality attributes remain compliant. Whilst Level 1 control greatly reduces the chances of producing out of specification material, the technique requires a high degree of product and process understanding [35].

Level 2 – Uses pharmaceutical control with appropriate end product testing.

This technique allows for flexible raw material attributes and process parameters within an established and defined design space that ensures product quality.

Level 3 – Employs tightly controlled raw material attributes and permitted process parameters.

The Level 3 technique requires less process understanding, relating to the impact of raw materials and process variations, on the final product quality and relies extensively on end product testing for release.

To date, we have seen more examples of Level 1 & 2 control strategies being applied within the industry.

What is a 'State of Control' and how does it Differ from 'Steady State'? As outlined in the U.S. Guidance for Industry [36], a state of control is described as one where a set of controls consistently provides assurance of *continued process performance and product quality*. For a continuous process, the controlled variable(s) depend on the control strategy employed, for example in a Level 1 case where process parameters can be adjusting to correct for changes/disturbances, a control parameter could be a quality attribute that is monitored in real-time. For a Level 2 case this could focus on the monitoring of raw material attributes and process parameters within defined boundaries.

In comparison, steady-state refers to a state where no changes are occurring – however the parameters of operation may not be those that lead to the targeted product quality and clearly this cannot be achieved in cases of Level 1 control. The term state of control is therefore preferred.

When comparing to a batch process that leaves a state of control, far less material is affected when utilising continuous manufacturing – this can have significant savings when considering the impact on time and cost. Should a process leave a state of control the material in process must be diverted – either to waste or to a holding area for further analysis. It should also be decided if the process should be stopped or diverted to waste, with collection only recommencing once a state of control is restored.

When telescoping steps, they can have different requirements in terms of reaction time, it can be considered to employ buffer vessels between continuous flow reactors to allow an upstream deviation to be dealt with without affecting downstream steps. Surge vessels can also be used to separate material that is not produced in a state of control. Managing process disturbances and how to deal with material generated during the transient states of start-up and shut-down sequences must all be decided on forehand and form part of the production protocol.

Use of Process Analytical Technology (PAT): From the definition of a control strategy it can be seen that process analytical technology (PAT) has a significant role to play within continuous manufacturing as it gives a real-time view of how a process is performing and if the material produced is of the required specification. The FDA considers PAT to be a mechanism of designing, analysing and controlling manufacturing processes by use of timely measurements. PAT is used to determine critical quality attributes of raw materials, intermediates and products; with again, the overall goal being to produce quality materials. An excellent review on the topic of PAT was recently published by the members of the IQ Consortium [37].

It is however not just a technique for manufacturing, within process development PAT is advantageous as it allows increased process understanding to be obtained and subsequently allows identification and definition of those parameters that will give a state of control when transferring the process to manufacturing. Within a manufacturing environment, the requirements of a PAT tool may change to be more specific and they are largely used to assess if you are operating within the defined process conditions (state of control) and if the resulting product is of the pre-specified quality – deviation from this will result in warnings/alarms based on the defined control strategy. Examples in the literature are wide ranging and include the use of NIR to determine water content in a process and for monitoring and controlling crystal form, together with a demonstration of online HPLC for a continuous hydrogenation by Lilly [38,39] and more recently conductivity sensors by GSK. As previously described the combination of PAT and continuous manufacturing techniques is taking manufacturing towards a situation of real-time-release testing (RTRT).

The different roles for PAT can be summarised as;

1. For process understanding
2. Higher level monitoring
3. Release purposes

Details of how you plan to use PAT should be given in your dossier that is submitted to the appropriate regulatory authority.

Quality Risk Management: When performing process development with a view to using the methodology for material production, key is to understand the process sensitivity towards change and disturbances. With this in mind quality risk management should include;

Risk Assessment: Ensuring that a fundamental understanding of the risks on product quality exists and that process dynamics are characterised relating to; material properties, equipment design and process conditions.

Risk Control: A control strategy that determines system health and product quality in real time is required (see above for a more detailed discussion of control strategy).

Risk Communication: This involves the development of methodology to deal with the increase in data that is associated with continuous manufacturing. Data needs to be analysed, used and communicated appropriately and not just collected! Procedures must exist on forehand that determine what will happen when a warning is received or an alarm is raised. The review of data also provides an opportunity for continuous improvement of a manufacturing process as time goes on.

What about Downstream? Whilst not the focus of this whitepaper, the reader should be aware that activities in continuous manufacturing are not only focusing on the reaction step(s), with Vertex [40] and Johnson & Johnson [41] receiving FDA approval for continuous tableting lines of Orkambi (July 2015) and Prezista (April 2016) respectively. In a publication from MIT, a consortium focussing on 'pharmacy on demand' also report the successful demonstration of the synthesis and formulation of a range of drug products including Valium® and Prozac® [42]. The resulting liquid formulations were found to satisfy US Pharmacopeia requirements.

Outlook & Challenges: With overwhelming publicised support from regulatory authorities, we see that the field of continuous manufacturing is moving rapidly, with adoption rates increasing at the kg, 100's kg and multi-tonne scale.

From a commercial standpoint, smaller equipment and facilities are attractive, together with the possibility to produce just in time, significantly reducing the costs associated with inventory of intermediates. Replication of production units also gives the possibility to deploy manufacturing set-ups, which are validated at the point of process development, to other parts of the world as a finished system. This gives better process control and robustness, together with lower batch-to-batch and location-to-location variations.

Depending on the sector that you work in and the scale at which you work, the drivers for implementation of continuous flow may vary. Currently, the following advantages are most often cited as reasons for employing continuous flow techniques;

- Low material consumption for process developments
- Minimised scale-up effects
- Control of hazardous reactions
- Improved product selectivity
- High resource efficiency
- Flexible production volumes
- Small footprint systems capable of operating at the tonne-scale
- Reduced costs

Bottom line is, do you have appropriate control to give you the target product in the required quality and safely?

Whilst the Asian market is moving more quickly, Europe and North America are following. Bruno [43] of Chemical & Pharmaceutical Solutions highlights the known '*high attrition rate in drug development*' and '*assets in the ground*' as being the biggest thing holding the industry back when looking to the growth of continuous manufacturing. The latter point is evidenced by the contrast seen

between developed and emerging countries, where no infrastructure is in place a process is directly developed with the view that both batch and flow are a viable option. The most suitable equipment is then selected as the solution!

Public-private partnerships have to date been instrumental in the development of early promotion cases of moderate scale continuous production, with most projects focussing on the development of modular 'skids' or 'container' based concepts. Examples of such completed projects include F³ Factory [44,45], INVITE [46], Copiride [47] and Coriac [48]. Active projects include CCFLOW [49] and ATOM 2 [50] which focus on the set-up of centres of excellence. Pre-competitive sharing of information has also advanced the field with initiatives like the working groups of ACS GCI Pharmaceutical Roundtable [51] and IQ (International Consortium for Innovation and Quality in Pharmaceutical Development) [52] having significant impact.

Technology road mapping can be one approach to deal with rapid technological changes and developments, allowing the links between technological resources and their effective implementation to achieve business goals to be defined [53]. Going forwards it is essential that CRO's and CMO's more widely adopt the technology as players in major Pharmaceutical Companies are looking for outsourcing and partnership opportunities.

On a final note, the importance of training cannot be stressed enough – if students are not taught the techniques, the next generation of development and process chemists will enter industry with the same toolbox that has been available for Centuries – the result being that they will invariably turn to batch and 'solve' their processing problems by altering the chemistry. At Chemtrix, we have worked together with many academic and industrial partners to deliver tailor-made theoretical and practical training. Successful implementation of continuous manufacturing results from a knowledgeable, multi-disciplinary team which builds on the strengths of chemists, chemical, mechanical and software engineers, together with quality and regulatory members to achieve the goal of robust process development and high quality material production. Possibly most importantly, the approach requires the intended users to embrace change.

Collaboration both internally and externally is key to success!

Additional Resources: For more information on how to get started with continuous manufacturing contact us at info@chemtrix.com or visit www.chemtrix.com for product and application information.

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