DECHEMA VDI

Modular Plants

Flexible chemical production by modularization and standardization – status quo and future trends

ProcessNet

EINE INITIATIVE VON DECHEMA UND VDI-GVC

IMPRESSUM

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Preface

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The European chemical industry is facing a strong global competition. With that, speed is becoming a more import end competition advantage. Speed requires agile innovation processes and quick investments in new production assets. Future production assets need to be as flexible as possible, such that they can easily be reused for new or modified products. A promising concept to improve competiveness and flexibility at the same time, especially for small to medium scale production, are modular production plant concepts.

The experts across chemical industries agree that such modular plant concepts have large economic potential. General concepts for modular production and the required enabler technologies for process intensification have jointly been developed in recent public funded projects, for example F^3 Factory, CoPIRIDE or ENPRO. These projects have shown that multiple challenges exist.

At the moment, there is a lack of standardization for modules on equipment level, as well as on the level of a complete production plant. Therefore, current modules cannot simply be bought on the market, even though it is broadly accepted in the chemical and pharmaceutical industries that this would result in significant advantages in investment costs, time to market and flexibility of production assets.

Associated with the non-availability of ready to use equipment and plant modules on the market, is the unmet market need for process control and automation concepts for modular plants. Additionally, the discussion of centralized (classical) process control systems versus distributed (modular) process control systems has just begun. The supporters of a completely modular design strategy envision the various plant modules acting fully automated and autonomously, with communication existing only via interfaces and communication protocols. Clearly this would be a giant leap forward towards full exchangeability and re-usability of modules. Having an appropriate concept for modularization of process control and automation could become one of the key enablers for modular production plant concepts.

There is also need for further development in the field of equipment/apparatus design, e.g. for separation and purification steps, that is available in different sizes in order to quickly and directly be scaled-up from laboratory to production scale at an acceptable risk. An often discussed, a simple and safe solution for production scale, is number-up instead of a classical scale-up. However, limitations exist as numbering up in many cases can increase investments costs and complexity significantly. The dilemma for the industrial process developer in this situation is the lack of clear design rules and guidelines to decide from an early phase of an innovation project whether a traditional scale-up concept should be followed, and increase the size of the process apparatus, or whether it would be smarter to use a numbering-up strategy.

To foster the cross company and cross university discussion and cooperation on modular plant concepts the ProcessNet Working Group “Modular Plants” has been set up. It includes the companies BASF, Bayer, Clariant, Evonik, Invite and Merck as well as the universities Ruhr-Universität Bochum and TU Dortmund. In this white paper the experts from the working group summarize the status of the discussion and highlight the fields where there is still need for development. I hope that this white paper inspires the reader to new ideas and encourages a cross chemical industry spirit of innovation for modular production plant concepts.

Frankfurt, December 2016

1. Motivation

This white paper is a common initiative of the ProcessNet Temporary Working Group on "Modular Plants" including the companies BASF, Bayer, Clariant, Evonik, Invite and Merck as well as the universities Ruhr-Universität Bochum and TU Dortmund. Recently finished public funded projects demonstrated successfully the technical and economic benefits of modular plants for the first time and their applicability especially for small to medium scale (typically 0,1 – 1000 t/a) continuous production [1]. However, further demand for development was especially identified in the course of industrial demonstration. Technical implementation of continuously operated plants was found to be more complex and challenging than conventional batch plants. Therefore, in addition to substantial process optimization, the nature of plant engineering and construction needs to be adapted to fully leverage the benefits of a continuous production approach for fine and specialty chemicals as well as pharmaceuticals. The paper targets all industries affected by modular plant engineering, e.g. other operating companies, equipment suppliers, automation companies and engineering companies. It shows remaining gaps, identifies need for further research and development and addresses the main challenges of this topic.

Today, the European chemical industry is facing increasing market competition from outside Europe and challenges with product launches in new and often volatile markets, i.e. among others a fast response to market requirements and reduced investment risk for new plants. Furthermore, shorter product lifecycles and thus smaller product volumes can be observed. These result from a diversification and increasing specialization of the product range due to more and more customer-orientated products. The latter

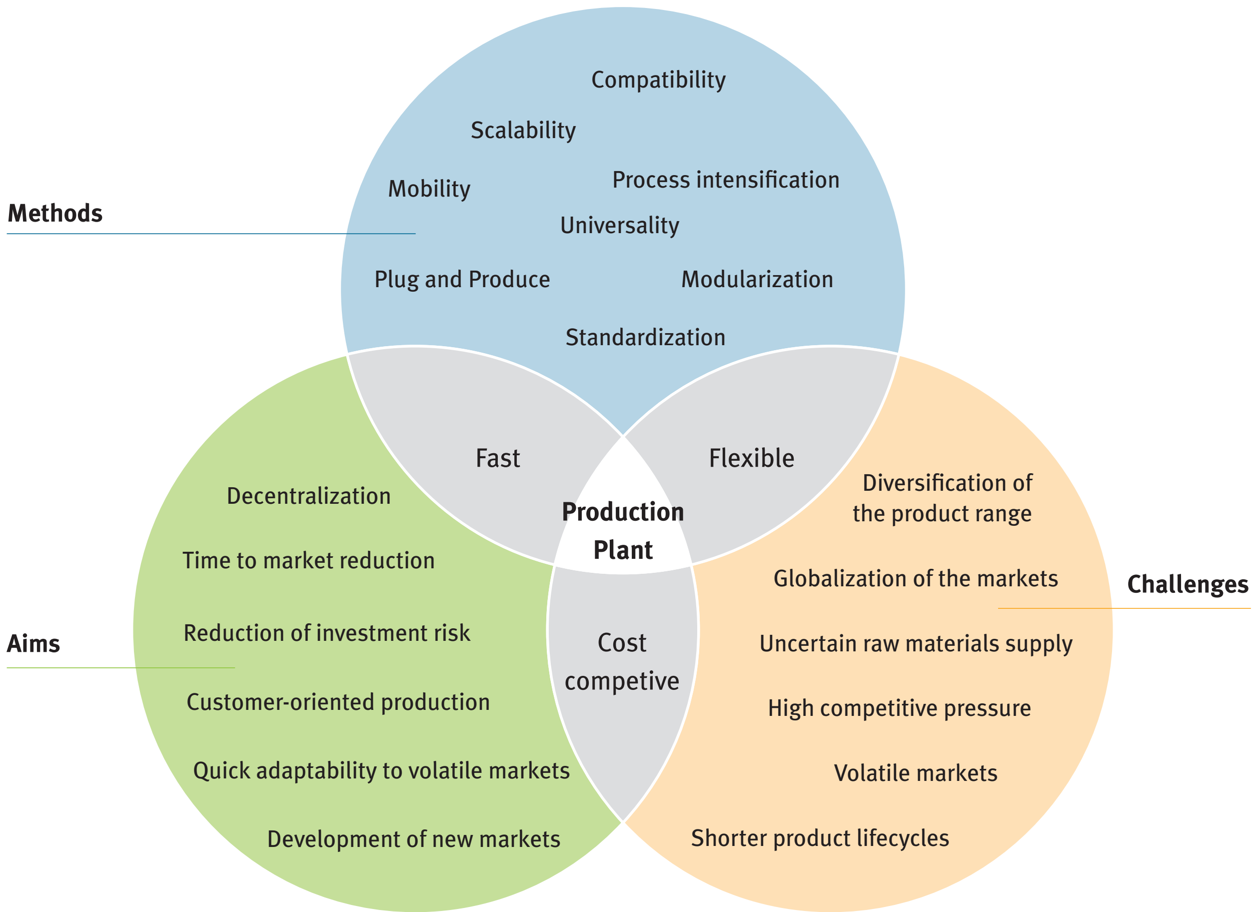


Figure 1: Methods, aims and challenges of reconfigurable production plants [2]

is further enhanced by the upcoming 4th industrial revolution (Industry 4.0). With this, the interconnection between customer and production is expected to increase thus asking for shorter delivery and development times (equals reduced time to market) and a quick adaption of the production set up to changing market and product needs. Figure 1 gives an overview of the methods, aims and challenges identified in this context.

In summary, it can be stated that flexible and cost competitive development methodologies and production technologies are required. To be successful in specialty and fine chemicals these methodologies and technologies have to be applied quickly. These boundary conditions can be met by applying modularization and standardization concepts to chemical process technology. Modularization can increase flexibility in terms of capacity (e.g. by numbering-up or parallelization), product mix (e.g. by exchange of reaction or downstream processing modules following a plug and produce), feedstock and site (e.g. mobility of modules). With standardized process technology, fast and cost competitive access to relevant process modules can be achieved. This is the case if standard modules are used by many companies and thus can be manufactured at a high number and lower costs.

Following these drivers, the European Commission invested jointly with their industrial partners approximately 100 million euros into research and development programs focusing on advanced manufacturing schemes over the last years. Micro reaction technology, process intensification, resource efficient continuous chemistry, modularization and standardization were key elements of the activities funded. The funded projects propelled the understanding of potential chemical and technological solutions for modular and standardized production plants. Additionally, as a result of research within the projects and an intensive precompetitive exchange among the industry partners, insight into both opportunities and constraints of the technology platform has been measurably improved, leading to subsequent research and development activities.

More general modularization frameworks with a focus on medium to large production facilities are currently being developed in projects such as the ENPRO initiative (Energy Efficiency and Process Intensification for the Chemical Industry) [3], which will provide the required engineering software for data integration and information exchange [4] throughout the plant lifecycle and between projects. In biopharmaceutical production, modular plant concepts with single-use systems are gaining importance. The special issues in this field are addressed by the DECHEMA Working Group "Single-use-technology in biopharmaceutical manufacturing" [5]. Figure 2 summarizes the drivers mentioned.

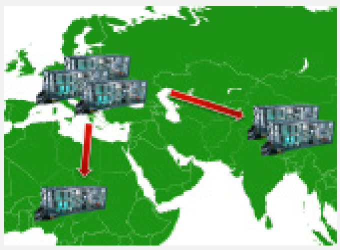
... Time to Market

- Faster plant planning due to reuse of information and workflows
- Savings in procurement and construction (known parts and vendors)

... Changeability in Production

- Compensate lack of flexibility of continuous plants using adaptable modules
- Achieve economy of scale enabling multi-purpose continuous plants

... Mobility and Risk Mitigation



- Distributed production nearby the customer / feedstock
- Sequential numbering-up of modular plants, following the market development

Figure 2: Drivers for modularization in small scale continuous production

Beside the strengths and drivers for the development and construction of modular plants, there are still challenges and weaknesses that require improvement of existing planning and designing strategies. The SWOT-analysis in Table 1 shows the position of modularization towards market competition.

As can be taken from the above mentioned considerations, the overall modularization concept affects nearly every step in planning and designing a chemical production facility. In Figure 3, the different chemical sectors (pharma, specialties, bulk chemicals and petrochemicals) are distinguished according to sector specific characteristics like capacity, chemical steps, product prices, environmental factor, the time to market and the plant concept. The white paper at hand focuses on modularization and its application to small to medium scale, continuously operated multi-purpose production plants. This is not a general restriction and other fields of application are possible and reasonable, but for technical (e.g. spacetime yield and compact construction in case of continuous production) and economic reasons the first focus lies on the currently most promising applications. The corresponding field of applications is marked with a grey frame in Figure 3.

Table 1: Strengths, weaknesses, opportunities and threats of modularization and standardization

Strengths (S)	Weaknesses (W)
» Improved flexibility, efficiency and profitability by reconfigurable multi-purpose production plants » Smaller CapEx by reuse of modules addressing short product cycles » Capacity expansion by numbering-up/smart scale-up » Accelerating engineering cycles by reusing know-how » Storing knowledge in documentation for future applications » Acceleration of construction, testing and operator training by utilization of centralized manufacturing capabilities » Easier realization of closed containment (e.g. for low environmental impacts) possible due to small scale	» Extra effort for the first implementation and maintenance of a modular engineering approach (e.g. databases, software support) » Extra effort for the design and construction of module prototype through essential guidelines » Restriction of technical opportunities due to design guidelines and conflict of goals (e.g. process optimization/standardization) » Available standard solutions may inhibit the application of innovative solutions » Limited applicability to world scale plants (losses in economy of scale)
Opportunities (O)	**Threats (T)**
» Platform technology for a broad range of applications » Fast provision of a demand-actuated production plant and fast entering of new markets and regions » Decentralized, resource-efficient production plants » Reduction of investment risks » New engineering and construction approaches, e.g. lean engineering and broader supplier market » New business opportunities, e.g. planning, maintenance, service, leasing of modules for suppliers or engineering companies	» Rate of reusing remain low (special solutions) » Insufficient attainable reconfigurability » Risk of know-how loss » Different local regulations vs. standardization » Low acceptance of innovative plant concepts

The required working areas and technology gaps identified in recent research projects (e.g. ENPRO, F³ Factory, CoPIRIDE, etc.) are described. Based on these, common activities of owners, operators, equipment suppliers and R&D centers are discussed that are necessary for a successful implementation of modularization in the pharmaceutical and specialty chemicals industry. Apart from the R&D demand, innovative business models are presented.

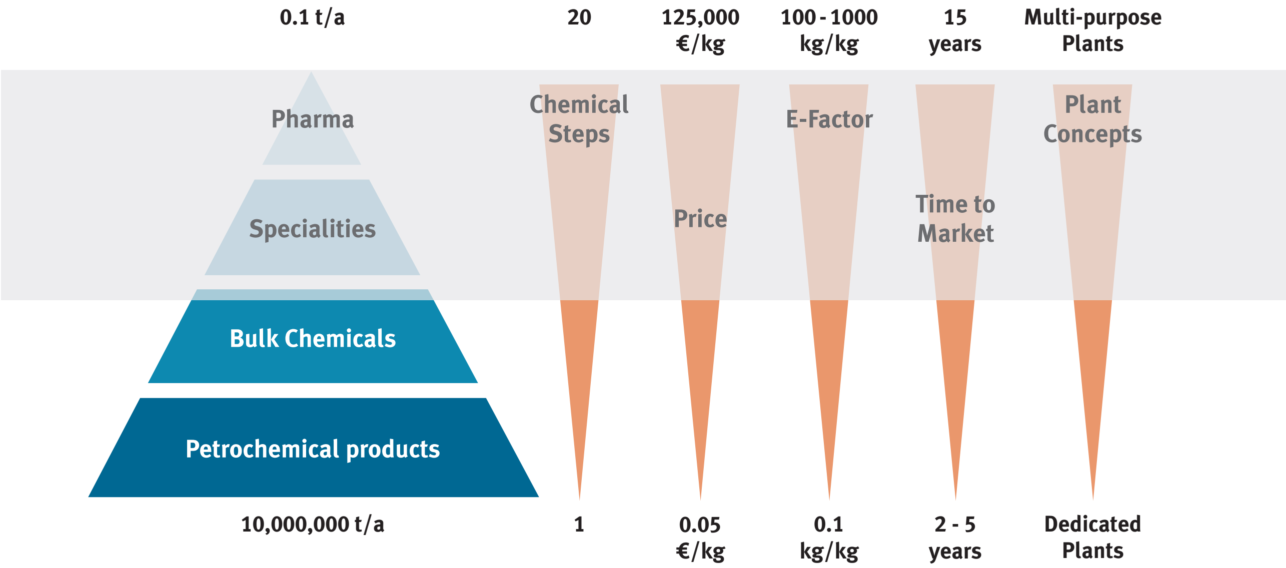


Figure 3: Applicability of modular concepts [6]

2. Status Quo

Following the motivation of this paper, the concept of continuous production with flexible modular plants is a promising approach to meet these challenges mentioned above. In recent research projects the technical and economic potential of modular production plants has been demonstrated. Modularization plays the key role of this concept and will be defined for chemical process industry in the course of this paper as

„Designing with standardized units, dimensions or interfaces, which can be easily assembled, maintained as well as flexibly arranged and operated“.

This section presents the current situation regarding modularization on different levels from planning aspects to physical modularization and reviews the results from the F³ Factory project, further developments and industrial implementation.

2.1 Concepts and Levels of Modularization

An accelerated engineering phase and a shorter time to market can be realized by the reuse of engineering information and closed data handling throughout the project phases planning, construction, operation, dismantling and reuse (Figure 4) [7]. This accounts for information on process equipment as well as for engineering workflows and plant design. To achieve this goal the utilization of a standardized, modular planning workflow is essential prior to physical modularization.

In order to address reconfigurability in production and to enable decentralized production, a physical modularization of process plants is offered in addition to the modular planning workflow. This physical modularization can take place on the level of apparatuses, plants, and logistics on site as well as in the production network [8]. If a physical modularization is desirable, the compatible modules are constructed as adaptable units and are assembled to form multi-purpose plants. During the following operation, the exchangeability of single modules simplifies maintenance and service and reduces changeover times. Operational data obtained during production can be directly used by

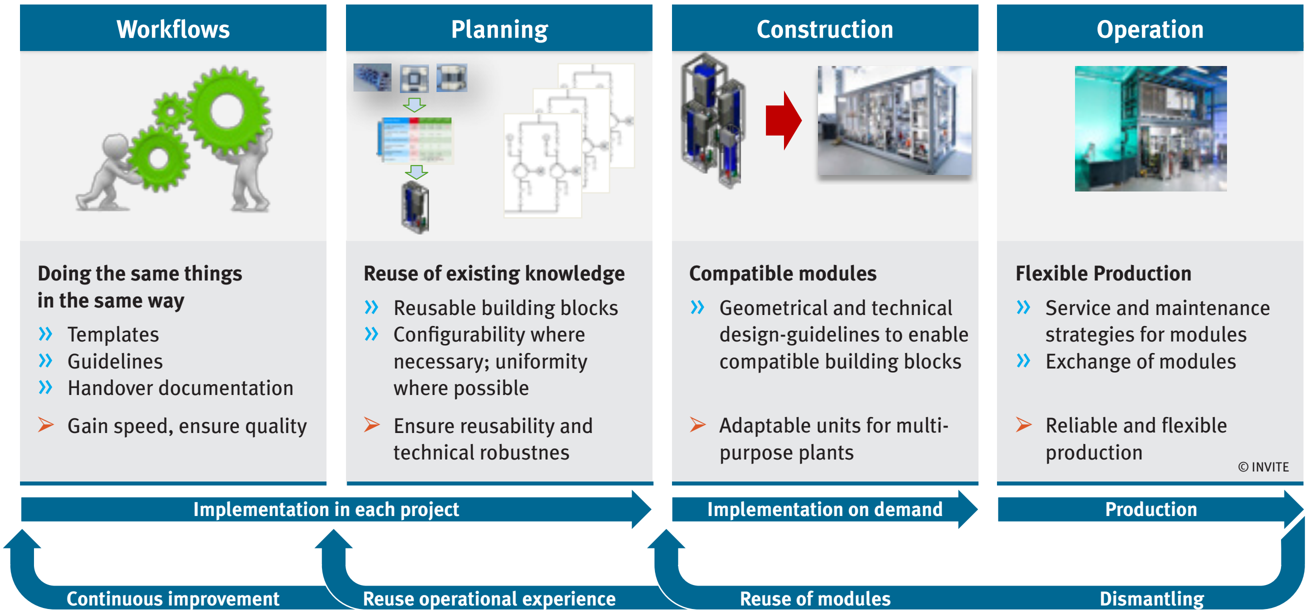


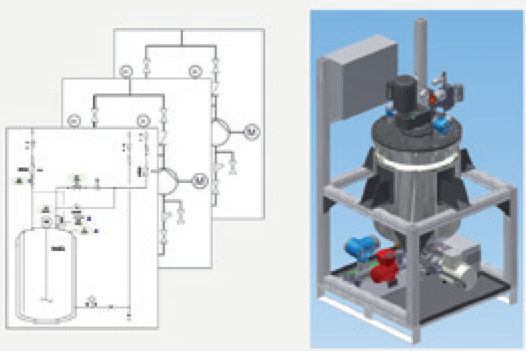
Figure 4: Procedural layers of modularization

the plant engineer to define maintenance strategies and to optimize already planned modules for prospective projects. Following the production phase, the plant will be dismantled while information and physical components can be reused. This ensures the continuous improvement and the reapplication of operational experience.

2.2 Modularization in Engineering and Plant Lifecycle

In order to enable the reuse of engineering information, a systematic modularization approach covering the process development up to the dismantling of a plant has to be applied. Therefore, a process is first virtually divided into equipment groups that belong to the same part of the process. This generation of modules reduces the complexity of a process and creates reusable building blocks. All planning documents required for the construction of such modules are merged in functional process units that we call Process Equipment Design modules (PED) which are saved in databases. A PED incorporates at least one main equipment item, providing the desired unit operation together with all needed peripheral components (e.g., pumps, heat exchangers, piping and process control components). The individual components are combined to achieve a desired PED operation window defined by technical parameters (e.g. ranges for temperature, pressure, flow rates, material grades). Within each PED the main equipment items can be exchanged to adapt the PED

Process Equipment Design (PED)



Documents in engineering and plant lifecycle

- PED contains one or more unit operations and all needed peripheral components
- Technical design guideline
- P&ID, Lists, 3D-CAD, cost estimation, models...

➢ Reuse of engineering information

Figure 5: Process Equipment Design

to different operating conditions. Each PED is stored as a database element containing all information and documents. The database needs to encompass the entire period to cover all project phases from initial planning steps to the operational plant, i.e. from conceptual design via equipment specification in basic and detail engineering until procurement and construction as well as plant operation and maintenance. In addition to typical engineering documents (e.g. P&ID, instrument datasheets, 3D-CAD...), it has to include templates for the process control system, a safety and reliability assessment and a list of possible configuration alternatives. Regarding the process life cycle, PEDs can help to accelerate the development from a research state in the lab to pilot and production plant. This can be achieved by numbering-up modular equipment or by using available equipment with the same functionality and main characteristics at different operational scales.

PEDs should be accompanied by simulation models, which allow for the configuration of modules, starting from a description of the PED functionality. The final goal for the application of these simulation models, is a definition of the PED´s operation window under given process boundary conditions.

Consequently, for an improved reuse, the PEDs are categorized in functional units, the process and service units. Process units are in direct contact with reactants, process or waste streams (e.g. storage and dosage, reaction, downstream, formulation and packaging). Service units have supporting functions for one or more process units, such as utility and energy supply, and do not have direct contact to the process streams. This distinction and the related database should allow for different reuse scenarios to speed up the time to market. If process specifications for a given task fit into an already existing PED, it can be reused without modification. If no existing PED will meet the specification of the process task under consideration, a new PED has to be designed. Therefore, the documentation package of the best fitting PED is used as a starting point and new components are specified where necessary.

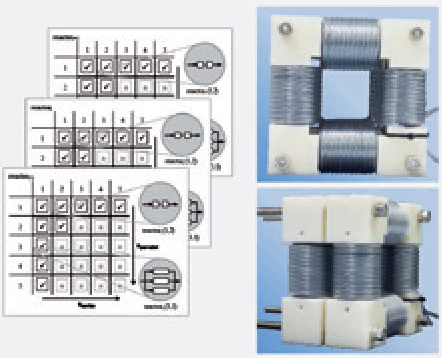
Single PEDs can be combined to form a Process Plant Design (PPD). The PPD conforms to the scope of performance of a modular plant and comprises all documents that are needed for a successful construction and operation (e.g. safety certificate of the combination of PEDs, summary of all maintenance and spare parts information of each PED to an overall maintenance concept, etc.). It defines the positions and connections between PEDs and virtually represents the desired process. Additional information such as P&ID and 3D drawings for the whole plant as well as possible operation windows of the single PEDs are stored in the PPD. Furthermore, due to the bundled information of each PED, the PPD enables a quick reconfiguration of the process by exchanging single PEDs. Once a PED is exchanged, the operation window of the PPD is adapted automatically. This approach supports the concept of reconfigurable production plants.

2.3 Modular Equipment

To enable an efficient, yet versatile production environment, the availability of reliable process equipment for industrial small scale processing is a fundamental prerequisite. This includes validated model descriptions for process-intensified equipment as well as robust devices providing industrial grade reliability. Modular equipment (ME) can help to standardize and facilitate equipment selection. Reusability to reduce complexity is especially promising on this level. A single piece of equipment can be defined as modular if it provides one of the following features:

- Inherent modular design, providing serial or parallel numbering-up of basic elements (e.g. channel reactor prepared for numbering-up of channel number and length) or another key feature dedicated for reusing the equipment.

Modular Equipment (ME)



- Serial and/or parallel numbering-up
- Configurable elements
- Series of equipment (same functionality at different operational scales)

Figure 6: Selection and configuration of Modular Equipment

- Inherent modular design, providing configurable elements to adapt to various operating conditions (e.g. modular process control systems providing variable integration of modules into the master system).

- Series of equipment providing the same functionality at different operational scales (e.g. a pump series providing different volumetric flow ranges utilizing the same operational principal).

2.4 Physical Modularization

In order to achieve versatile continuous production units and to enable decentralized production, a physical modularization of process plants can be applied. Module definitions will then be performed such that functions defined in PED definition are maintained. Physical modularization is suitable for multiproduct/multi-purpose plants, in which frequent reconfigurations of the process structure are common between production campaigns. Additionally, an integration of small scale continuously operated equipment into pilot or multi-purpose batch plants can be realized to enable highly efficient hybrid production concepts. In this case, the plant consists of individual Process Equipment Assemblies (PEAs). A PEA represents the physical implementation of a PED, following additional geometrical and technical design guidelines, to ensure compatibility of independently planned modules. In addition, each PEA contains its own automation and control intelligence that interacts with the other PEAs via defined data interfaces. Near-field process control systems are provided, which can be connected to the overall process control system. PEAs can be exchanged in operative conditions of the plant, via defined physical interfaces to allow a versatile retrofitting for multiproduct- and pilot-plants. Each PEA is constructed into a transportable skid in which the footprint of the skid is a multiple of a discrete grid size, which gives flexibility for the arrangement and rotation of adjacent modules. To enable fluidic and electrical connections predefined compartments as well as standards for the final interconnection of the PEAs are specified. Especially for the main equipment, a certain void space inside each module is reserved during initial planning, which allows for integration of different equipment configurations without major design reviews, in order to facilitate the reuse of already planned PEAs.

The connection of various PEAs to a production plant is described by the Process Equipment Frame (PEF). The PEF contains the geometric conditions and safety-related specifications of the installation environment and covers the supply of all PEAs. Containing the overall process control system of arranged PEAs the PEF is considered as an independent production unit. For standalone or decentralized production scenarios, the integration of PEAs into a PEF can be performed in modified freight containers, which can provide a fully integrated infrastructure to build up a mobile and reconfigurable production environment, requiring only basic utility supply on site. In this case, the PEA design is subject to geometrical specifications.

2.5 Infrastructure and Utilities

The modular concept is completed by an appropriate modular infrastructure, in which the PEFs can be integrated and operated. This infrastructure should provide access to the utilities the PEF requires, e.g. via a standardized backbone interface. Required utilities could be pressurized air, nitrogen, raw materials, waste streams as well as necessary data connections. It could also deliver an interface for the supervision and orchestration of the PEAs and PEFs via a so-called “Process leading level”. The modular infrastructure further provides the basic structural needs such as light, accessibility for frames and ventilation. The latter do not necessarily need to be appropriate to operate the frames without additional ventilation for EX-proof processes. However, it should be possible to operate the PEAs and PEFs not just for R&D activities, but also for production purposes. Thus, the infrastructure needs to be qualified as a production environment (e.g. permissions, etc.).

Finally, the extended modular infrastructure comprises the whole site including a logistic concept for the PEAs and PEFs (e.g. warehouse) as well as service aspects (e.g. maintenance).

A special infrastructure to house small PEAs could be a standardized container that provides the necessary infrastructural components as mentioned above. Evonik developed such a standardized mobile infrastructure platform called “EcoTrainer” that is capable of housing and operating small-scale, modular processes.

2.6 Analytics

To take full advantage of intensified continuous processes, key steps must be taken towards long-term stable, tightly controlled and fully automated production. In this context, process analytical technologies (PAT) play a crucial role. Based on their information the critical process parameters (CPP) can be monitored, controlled, and optimized in order to achieve the desired product output quality or to detect changes in critical quality attributes (CQA).

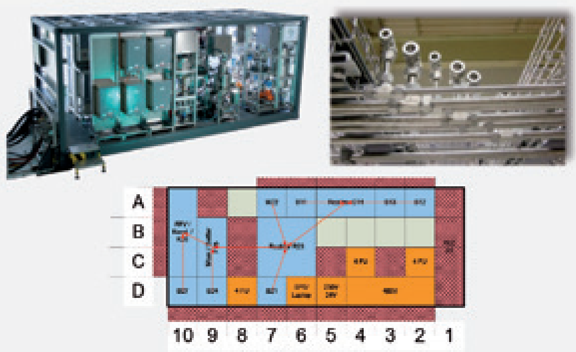
To enable an efficient implementation of PAT tools, the required measuring methods (including appropriate measuring/sampling points) should be defined at an early planning phase. Ideally, the same analysis methods are applied throughout process development and scale-up from lab to pilot or production scale. This makes an accelerated implementation of PAT tools possible.

Process Equipment Assembly (PEA)

Physical representation of PEDs

- Follows technical and geometrical guidelines
- PEAs for unit operations and support functions
- Providing functional modularization
- Reusable, replaceable and combinable elements

Process Equipment Container (PEC)



Frame for plants containing individual PEAs

- Installation and fixation of PEA
- Connection and distribution of energy, utilities and process media
- Adaptable production units
- Mobile embodiment

Figure 7: Process Equipment Assembly and Process Equipment Frame

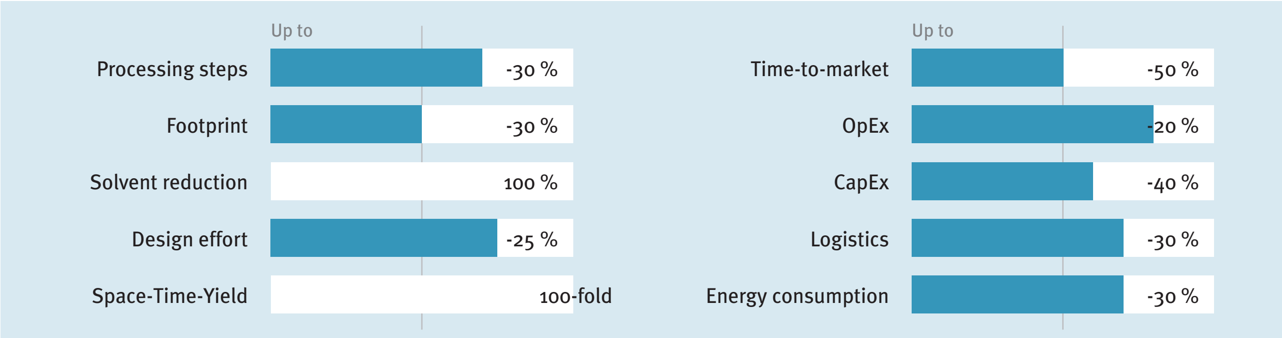


Figure 8: Modularization and intensification showed measurable impact from F³ Factory Project [11]

The strategies, developments and claims of the process industry with regard to PAT tools mentioned in "Roadmap Prozesssensoren 4.0" [9] can also be applied for small-scale, modular plants. Especially the ATEX (ATmosphères EXplosibles) confirmation of PAT tools, the close arrangement of measuring point and sensor, and the integration to the modular automation are specific aspects and demands for modular plants.

Some of these issues are currently addressed in the EU-funded research project CONSENS (Integrated Control and Sensing) [10]. The goal of the CONSENS project is to advance the continuous production of high-value products (meeting high quality demands in flexible intensified continuous plants) by introducing novel online sensing equipment and closed-loop control of the key product parameters. Innovative process analytical technology will be developed for online concentration measurements, for the online non-invasive measurement of rheological properties of complex fluids, and for continuous measurements of fouling in tubular reactors.

Modular Infrastructure (MI)

Integration of PECs in a modular infrastructure

- Standardized provision of required utility and raw material supply via a backbone
- Supervision via a higher process control system
- Necessary site logistics
- Production environment

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Figure 9: Modular infrastructure

2.7 Proof of Concept

F³ Factory and learnings

The F³ Factory project followed a completely new approach for planning and designing modular plants. The vision was a radical modular approach for a rapid process development, the implementation of novel flexible and sustainable processes with an improved CapEx (capital expenditure) and OpEx (operational expenditure). In the successful case studies, the potential of intensification and modularization for the chemical industry was demonstrated. The numbers quoted in Figure 8 represent results achieved across the case studies of the F³ Factory project. The outputs of individual processes and industrial case studies may be different overall [1].

Despite the successful project, there are further results and lessons to be learnt (Table 2). During the F³ Factory project, first design guidelines and standards were applied that enhanced the flexibility of a production plant by exchangeable PEAs (e.g. standardized footprint; smallest grid element with a length of 570x570 mm [12]). With the defined standards, the consortium as well as the equipment suppliers had to design their equipment according to the technical design guidelines.

Industrial implementation

Besides public funded projects, chemical companies as well as suppliers have already started to implement modularization in their different fields of application. Lacking a common understanding of the degree of modularization and standardization, various ways have been used to implement modularization in these companies. The subse-

Table 2: Lessons learnt of F³ Factory

Successful	Weakness & Challenges
» Modular concept shown for a wide range of chemistry – Polymers – Surfactants – Intermediates & fine chemicals – Pharmaceuticals » Scale of tested applications – Tested range: 5 t/a – 120 t/a – Possible production scale: 0,1 t/a – 1000 t/a » Operational Aspects – Normal qualification for staff team – From truck to operational readiness in 40 minutes » Maintenance – Exchange PEAs in ~ 1 h possible	» Prototype challenges – Development of first PEAs and PEFs is time and cost consuming – Standardization still in an early phase – Benefits only available for developed PEDs » Backbone optimization possible » Equipment challenges – Robustness of equipment (e.g. pumps valves, ...) – Limitations for thermal separation steps » Currently only applied in niche markets » National regulations limit easy transfer of equipment to different countries » Technological gaps still existing

quent chapter emphasizes the interest of the individual companies and the need for further development.

While the evolution of modular plants is still in an early stage of implementation, container-based solutions are already applied for small-scale commercial production:

» BASF uses customized containers for small-scale production and its advantage of centralized construction workshops and subsequent transportation to the production site of interest.

» Evonik uses containers as a special kind of standardized mobile infrastructure platform (Eco Trainer) for fast process development and subsequent small-scale production. This concept has successfully been demonstrated for electronic chemicals in the past [6]. In addition, Evonik is establishing a modular frame concept similar to the F³ Factory concept for process development in a pilot plant environment.

» Merck is operating in an environment in which time to market is the most sensitive fact for introducing new products into the market. The small-scale continuous production plants follow the Multi Process Plant concept, which ensures a high flexibility in combination with process intensification.

» Clariant differentiates between modular plant concepts that address specific needs like market entry (fast & reliable) and types of technology transfer (sampling, piloting, and training). At present, Clariant is working on pilot projects with focus on formulations and chemical reactions.

» Invite offers engineering services for modular plants following the F³ Factory concept. This includes basic and detailed engineering as well as testing at a technical center especially equipped for modular process containers.

In addition to the implementation of these concepts in the chemical companies, there are more and more suppliers applying these concepts in their business. ZETON offers the construction of modular lab-, mini- and pilot plants for different chemical sectors. Integrated Lab Solutions (ILS) builds compact lab- and mini-plants especially for high throughput experimentation with ME. Hte provides technologies and services for enhanced R&D productivity with focus on high throughput technology platform and modular systems for catalyst testing. Lonza and Ehrfeld offer modular microreactor systems for continuous production. Furthermore, HiTec Zang developed a lab automation system that allows for a quick realization of batch sequence protocols. However, these modular concepts are still based on individual standardization concepts and lack a common standardization approach.

3. Required Working Areas and Gaps

Based on this status-quo a high degree in flexibility and efficiency has already partially be proven in the recent years by modular technologies such as micro reaction technology. Nevertheless there are some blank areas, which need to be addressed. The next step for a successful implementation of modular plants in the chemical industry is the identification of technology gaps and business challenges as well as the subsequent provision of sustainable solutions.

To ensure the exchangeability of PEAs, **standardized interfaces, standards in the modular automation [13] and an integrated PED and apparatus database/portfolio** are required. The technical feasibility of the adaptable, modular plant concept has successfully been demonstrated although there is still a need of a **standardized planning process.** The application of apparatus databases for systems modeling, reliability and CapEx estimation is a standard tool in chemical engineering. For small-scale innovative equipment the necessary information is not yet systematically classified or not even available. Therefore, a systematic database of equipment information as well as model-assisted tools for equipment selection in the planning process is needed [14]. After this extra effort for the first implementation has been spent, the engineering will be further accelerated and the storing of knowledge for future applications is possible.

In order to achieve this aim, **challenges within apparatus development** must be met. For the implementation of complete modularized processes, there is a special need for **small-scale, continuously downstream PEAs**, which match **geometrical limitations** (e.g. height of standard freight container) and fulfill the required separation efficiency. Additionally, due to the mode of operation and in special cases the small-scale geometrical dimensions of a modular plant, **the selection** of suitable **reactor designs, equipment and new sensors for reaction/product monitoring** is important to enable a **robust and reliable operation.** For the development of an innovative and efficient small-scale production technology platform, a close cooperation between owners/operators, engineering companies, equipment suppliers and R&D centers is mandatory.

Furthermore, **scale-up strategies** that support the definition of modules (PED, ME, PEA, PEF) and allow a scale-up in a time efficient way, are necessary.

Quick exchangeable PEAs enhance the flexibility of modular plants to produce different products in various capacities and represent an alternative to multi-purpose batch plants. To ensure an overall fast process adaption with low changeover times and reduced effort for plant operators, modular **automation concepts** must be developed.

To provide a demand-actuated production, **plant logistics and supply chain management** of modular production concepts must be supported by two aspects. Firstly, modular logistics handling units and appropriate processes have to be created. Secondly, planning methods on site and production network level have to be developed.

The advantages of positioning PEAs in a transportable skid (PEF, e.g. ISO-container) to enable decentralized production go along with challenges getting an operating license for a plant at different law fields **(regulations)** and **further boundary conditions, such as GMP** (Good Manufacturing Practice) ability or CE specifications. In addition, different local regulations may require designs contrary to the standardization guidelines.

Depending on the needs of the customer the degree of reconfigurability of modular plants can vary. Derived from business cases and products, the requirements of business and technology concept have to concur. Therefore, a standardized management model for choosing the suitable modular plant design that meet customers' needs has to be developed. **New business and service models** are required to exploit the flexible modular production in practice.

3.1 Standardization and Interfaces

Reduced stock ranges and just in time production will demand for new designs of chemical production facilities. In order to achieve an efficient design, process functions should be separated into standard functions and functions that need process understanding or that represent competitively relevant know-how. An efficient design process has to find standard solutions for standard tasks. These solutions should be prepared by suppliers so that the focus can be placed on the competitively relevant tasks.

Structuring a design problem into individual tasks is the fundamental idea of module based plant design. For these tasks, solutions can be found with defined boundaries and minimum interaction with preceding and succeeding tasks. A key prerequisite for this approach will be the development of standard solutions for problems occurring repeatedly and the definition of guidelines for designing new PEDs. Examples for standard applications are storage, dosing or mixing. These typically do not represent competitive knowledge and can be developed in a joint effort by multiple companies and manufactured by suppliers. This could substantially reduce plant manufacturing costs. On the other hand, PEDs will have to be designed individually or existing PEDs need to be modified, either because no suitable PED is available, or because certain boundary conditions make individual design inevitable.

In order to bring PEAs into operation, interfaces are required to interconnect PEAs among one another and to local infrastructure. In cases where the later plant will be operated in an environment especially designed for hosting PEAs, MI interfaces can be defined for mechanical, fluidic and electrical connections and for the communication with the process control system.

To guarantee PEA **compatibility and quick and easy plant reconfiguration,** interfaces have to match the requirements of a large variety of potential processes. This can only be achieved with flexible interfaces suitable for adaption to local boundary conditions. Even though interfaces have to be standardized for connections frequently applied, a certain degree of freedom is still needed to adapt the interface to local requirements. This will allow for a quick PEA installation and plant reconfiguration in multipurpose plants. In cases of frequent exchange, rigid interfaces are required that allow for quick PEA connection and disconnection. However, this may cause substantial additional costs. It will thus be important to find a reasonable compromise between standardization and flexibility. A universal interface applied for any type of PEA will not be reasonable. Only if interfaces are sufficiently flexible to adapt them to local boundary conditions, these standardized interfaces will be applied.

A **single purpose plant** in contrast does not require frequent reconfiguration so that module/module interfaces can be more flexible. It is sufficient to guarantee that local piping and wiring is able to connect the modules with each other. Defined connection dimensions and technologies as well as handover locations are required, both for mechanical and electrical or information interfaces. The focus must therefore be on the time and cost determining aspects of the overall concept. In cases in which module exchange is expected infrequently, it could for example be sufficient to describe the location of a hand over position of a connecting pipe in order to guarantee compatibility. The physical connection pipe however could be produced and tested locally if the rest of the module is already assembled and tested.

Manufacturing the PEDs will benefit from clearly defined interfaces and design guidelines because the number of iterations required during plant design will be reduced saving costs and time. When designing PEDs, brown field application like the extension of an existing facility should also be taken into consideration. The application of proven solutions is still reasonable, additionally skid design can be beneficial to allow for a quick installation. Interfaces have to be sufficiently flexible to integrate the PEA into existing piping and into the existing process control system. This will be especially important as a PEA will not only host the main equipment item, but also automation and other auxiliary equipment. PED and PEA standardization should focus on defining a spatial structure including the position of the main equipment item so that it still allows for flexible adaption of its interior.

Setting up a production facility from PEAs requires a determined **throughput corridor** for each PEA. Additionally, a clear description of the PEA structure in terms of spatial subdivision is necessary to fully exploit the benefits of module based production technology, e.g. using PEFs. **Safety aspects** will play a key role in module design. Allocation of intra-modular and inter-modular safety functions will require much attention. PEDs should be designed inherently safe, nevertheless module/module interactions have to be surveilled closely. When defining the **PEDs´ structure,** the demands of ergonomics, maintenance, changeovers and reconfigurations will have to be taken into consideration. For PEDs designed for operation in multi-purpose plants, cleaning capabilities will be crucial in order to avoid cross contamination. This will require interfaces for the supply of cleaning agents, waste disposal and for ventilation.

Summing up, the following **key activities** are necessary:

- As a first step towards standardization operating and engineering companies prepare specification sheets in a joint effort
  - for common process and service PEDs (e.g. storage and dosing, mixing).
  - analogously, for the definition of interfaces.
- Based on these specification sheets, suppliers develop the PEDs required.

3.2 Planning Process

The key difference between conventional and module based design is that potential equipment and its characteristics are already known in early design stages in case of module based design. In contrast to conventional design, this requires **equipment selection and process parameter adjustment instead of individual design.** Thus far, equipment is designed such that it meets the process requirements. Consequently, it may be required to adapt the individual process parameters per unit operation to available equipment instead. Here, **robust design and optimization strategies as well as tolerant unit operation design** are key. This can lead to substantial time savings but also to drawbacks in terms of process efficiency compared to a process individually designed. Designing a plant in a modular way may thus have a strong impact on the planning process. Therefore, the decision for or against modular design should be fixed in early design phases. As a consequence, an innovative planning approach is required.

A comparison of conventional and module based production approaches will only be reasonable if **all cost factors are evaluated** in a holistic production scenario. This includes the costs for the supply chain, personnel, size dependent equipment, changeover and many others. To evaluate such production scenarios new cost models are required. Especially important is the fact that ME will have a different cost structure than conventional equipment. ME must be designed for a wide operating range with robust design and tolerant unit operations and equipment. For the main equipment items, new design approaches will be required aiming at increased equipment flexibility. This will have an impact on equipment costs and therefore requires new equipment-cost correlations. For the auxiliary equipment, e.g. the number of measurement and control devices may vary. To allow for quick and precise investment cost estimation of the auxiliary equipment in early design phases, configurable, modular flow charts will be required. Here, development has proceeded already quite far. One example is a P&ID configuration using decision trees. Yet, new technologies for knowledge management and decision support will be required similar to those already available for car configuration.

The design process has to start with an **analysis of potential drivers for or against a modular design** concept. In the next step, process design has to take into consideration possible modular solutions and spatial limitations in the final plant. **Efficient selection** requires knowledge about potential solutions and the equipment available must fully be described by simulation models. Therefore, ME has to be characterized such that it is described for reuse including full documentation of possible configuration options. Additional to the opportunity for reuse, this will generate reviewed planning documentation with well-defined boundaries, helping to reduce iteration cycles common in state of the art planning. Furthermore, know-how collected in simulation models can be used for describing PED properties in life cycle management. This can for instance facilitate the communication between PEA manufacturers and operators.

Tools are required that allow for a structured equipment comparison and **selection.** These tools will have to be based on existing simulation models to describe the physical and chemical processes occurring. However, in modular planning, the final operating point can no longer be defined precisely. Thus, an equipment has to be selected that covers the best possible operating range. In order to allow for decision making, new tools are required that use simulation models of the equipment available for selection against the background of insecure data. In the recent past, tools have been developed for decision making under uncertainty in early phases of process development. Expanding these approaches to modular technologies will be required.

Even though the full benefit of modular planning can only be generated if PEDs for each unit operation are already available, which is not the situation today. Thus, **PED development** will be a key task for the near future. This can help increasing robustness of the planning process and make workload less cyclic for the planning teams.

Summing up, the following **key activities** are necessary:

- » Academia together with operating companies develop
  - the fundamentals of decision making in module based planning and design.
  - prototypes of simulation based decision support tools to
    - select ME against the background of insecure data.
    - take the decision for or against modular design in early design phases based on a sound economic comparison of conventional and modular design.
  - new, robust design approaches aiming at increasing equipment flexibility and process tolerance.
- » Engineering software vendors prepare the framework to implement the decision support tools developed by academia and operating companies.

3.3 Apparatus Development

In general, modularization is possible independent of new apparatus technologies but their implementation facilitates modularization. Therefore, the main challenges of apparatus development in this context are elaborated in the following sections.

Reactor selection and scale-up

New reactor concepts are an important enabler for small-scale plants. Special focus in the future is expected to lie on continuously operated reactors/processes for several reasons: high space time yield, low internal holdup, resulting in, e.g. small amount of toxic/hazardous substances or less waste in case of product changeovers, often inherently safe design is possible, more constant product quality and better energy integration, as well as broader accessible process window in terms of reactant concentration(s), temperature and pressure. The innovation needs in the field of reaction technology can be divided into the areas new reactor geometries & designs, new materials and manufacturing approaches for reactors, new sensors for monitoring the reaction and modularization/standardization of reactor equipment.

New reactor geometries and designs can handle very fast exothermic reactions, e.g. in nozzles, accompanied by highly viscous media, e.g. in case of a solvent free process. Solids dosing including bio raw materials is a challenge for small-scale equipment. Multiphase reactions can include complex behavior, e.g. phase transitions of reactants and/or products along the conversion axis. This includes paste processing or fully solid process media such as granules or powders from precipitation reactions. The novel reactors should be easy to clean or include cleaning-in-place concepts, e.g. for very toxic raw materials. For improvement, cleaning dead zones have to be minimized resulting in less/no fouling and narrow residence time distribution. To control heat release or reaction progress, distributed dosing should be feasible for reacting media, solvents, or additives along reactor walls or through internals.

New reactor materials and manufacturing approaches including additive manufacturing technologies enable the fabrication of new geometries for optimized reactor shape, faster development and testing of new reactors. From these suppliers, new spare part concepts and single use concepts can be offered. Alternative materials, e.g. ceramics for high temperature applications, can be fabricated with additive manufacturing for application in highly corrosive reaction systems. Furthermore, special wall coatings, e.g. anti-fouling or functionalized reactor walls can be fabricated to allow for novel process windows.

To monitor reaction outcome with conversion, yield and selectivity, **new sensors for reaction/product monitoring** should be integrated close to the reactor including analytics via auto-sampling. Typical sensing methods include spectroscopic methods or sound and vibration assisted by tomographic methods.

Modularization and standardization of reactor equipment should include, as already mentioned, an easy and flexible combination and reconfiguration of equipment modules. Intelligent PEDs should include local control systems autonomously running and "communicating" via information, material and energy streams. MEs should enable consistent scale-up, where lab-, pilot-, and production-scale equipment is fitting to each other. Similarly, equipment for special process conditions such as high or low temperature, or high pressure, should be easily configurable, so a direct scale-up is possible.

Fouling

Fouling is the unwanted buildup of material on a surface, for instance deposited particles or adsorbed macromolecules. Due to increased flow, heat and mass transfer resistances, blockage of flow channels or corrosion, several industrial sectors are facing tremendous losses of productivity and related costs of US$ 4.4 billion annually [15]. An important step to gain knowledge about the actual fouling behavior and to allow advanced process control is to measure the progress of layer formation and growth. The current state of the art for the detection of fouling consists of point measurements of the thickness of the fouling layer [10] by ultrasonic-based sensors. It can identify process conditions that accelerate fouling, and help to better understand fouling mechanisms. Moreover, it can be used to identify the ideal moment to clean the reactor in order to minimize downtimes. The fouling sensor is particularly beneficial for small-scale modular plants, since it can predict the fouling behavior during scale-up based on laboratory studies [16]. However, the integration of PAT in modular plants can be challenging. The equipment either has to be integrated into existing PEAs or dedicated process analytical PEDs have to be constructed. For certain processes, ATEX regulations must be fulfilled. Communication between the sensors, the control system and the plant must be established enabling an extensive use of the sensor measurements.

Downstream processing

The application of ME, especially downstream units, in PEFs with geometric limitations presents further development requirements in the modular plant design. In recent public funded projects [8, 17] the upstream processing with micro- and milli-structured, intensified equipment was successfully demonstrated. The situation differs when downstream processing (DSP) should be integrated in a small-scale PEF. Considering a range of 0.1 to 1000 t/a (0.0125 kg/h to 250 kg/h) as a typical production capacity, which complies with the design guidelines developed in F^3 Factory, it is necessary to identify suitable downstream modules. The application of thermal separation processes (e.g. distillation in a column or for thermal sensitive products the use of falling-film evaporators) in PEFs with geometric limitations quickly reaches its design limit, for example due to the required height. In general, a compact format is desirable for modular setup. In these cases, alternative strategies and ME for DSP have to be developed. Therefore, current continuous DSP concepts (for example described in [18] or [19] in small-scale or [20] in larger scale) have to be evaluated and classified according to the technology readiness level (TRL).

Solid handling

Solid handling represents a challenging area in the small-scale, continuous and modular production. When dosing powder, which is dosed in the laboratory either manually or by means of laboratory equipment or for large-scale processes by screw conveyors, pneumatic conveying, etc., there is a lack of dosage concepts that meet the typical requirements (e.g. continuous promotions, low feed rates from 0.1 to 20 kg/h, etc.). While lab devices are often not certified for ATEX Zone 1, apparatus for large scale application do not have a compact design. In addition there is a demand on robust isolation valves (DN ≤ 20), which ensure reliable continuous operation. In order to realize a continuous dosing in small-scale dimensions for the continuous production, there is a need for developing strategies and robust equipment in cooperation with manufacturers. This is an essential requirement for the next big challenge, an integrated end-to-end approach along the complete value chain of the production of APIs, for example.

Temperature management and heat insulation

For planning and construction of PEAs for PEFs, the available space has to be exploited effectively. If fluids with high or low temperature are transported, the pipes, fittings and equipment (sensors and actuators) require additional devices (double pipe, heating plates, etc.) and insulation. Additionally, in a compact process environment temperature control such as air conditioning could be crucial to prevent e.g. automation equipment from operation outside its boundaries and reducing its life time. Due to the fact that the application of water bath during the scale-up from lab to production scale is improbable, new strategies for temperature control has to be developed, which enable the temperature control despite small installation space. Depending on the chosen concept of temperature control (electrical heat tracing, heating/cooling with liquid media) a practicable PED layout has to be developed and functional equipment has to be identified.

Reliability

While the technical feasibility of the small-scale, modular concept has been successfully demonstrated in F^3 Factory project, it is challenging to choose suitable, robust equipment. During the scale-up from lab to production scale (capacity approx. 0.1 – 1000 t/a) equipment is used, which is more attributable to the dimensions of the laboratory. At the same time, however, it demands the reliability properties of a production plant (operating: 8000 h/a).

Especially solid dosage, small evacuation systems, compact DSP, control valves, etc. require further development.

Summing up, the following **key activities** are necessary:

- ME and PEA suppliers, operating companies and academia develop
  - new reactor geometries & designs, new materials and manufacturing approaches for reactors.
  - new sensors for monitoring the reaction regarding conversion, yield as well as selectivity and the plant condition regarding fouling.
  - compact equipment for downstream processes and for solid dosage on pilot plant scale.
  - temperature management and heat insulation concepts for PEDs with small installation space.
  - small-scale, reliable equipment such as control valves, small evacuation and solid dosage systems, etc.

3.4 Scale-up

A PED embracing a unit step of a chemical process with a database of design and process information starts from lab development over pilot to production scale [21]. Scale means length scale of equipment enabling certain volumetric throughput and production rate from grams to tons, but also time scale from short experiments to long-run tests and production campaign of several months. With increasing scale, fixed costs decrease compared to variable costs and lead to more economical production (economy of scale). ME consists of functional elements with standardized interfaces, e.g. reactor plates with mixing channels and standard fluidic tube connectors. Separation columns may have standard sections, which can be enlarged for higher throughput. Furthermore, ME may also include a batch process step within a continuous process. Scale-up of batch processes is mainly done by increasing the vessel volume with heating/cooling capacity and stirring/mixing characteristics. An increase in vessel volume is accompanied with a dramatic decrease in surface-to-volume ratio, leading to lower heating/cooling rates, longer mixing time, and probably lower reaction performance with side products or instability of exothermic reactions.

Development of a continuous chemical process starts in the lab and aims to design a production plant on the relevant size scale with desired throughput. When starting from a target molecule, process step or known batch protocol, a feasibility study is the first step to prove suitability of the chemical and physical system [22]. A **toolbox of existing**

Table 3: Scale-up parameters for modular equipment, a guideline

unit operation	constant for scale-up CTQ	important parameter	observed parameter CPP
mixing	mixing time	energy dissipation rate	pressure loss [26]
heat transfer	volumetric heat transfer coefficient	specific surface, flow rate, pressure loss	outlet temperature, temperature maximum
conversion	residence time	flow rate and internal volume	outlet concentration of starting material
selectivity	heat transfer; residence time distribution	Reynolds number, Peclét number	outlet concentration of impurities of side product
separation: distillation absorption extraction adsorption membrane crystallization	} separation efficiency crystal characteristics, purity	area for vapor flow area for gas flow energy dissipation rate } area to volume flow rate temperature/concentration	} outlet concentration [27] temperature, concentration, product quality [28]
solids handling:	formulation quality	speed of solids handling; numbering-up	process specific

PEDs with vessels, pumps, reactors, and separation steps assists the rapid development by replicating engineering knowledge [23]. A pump or a reactor ME, for example, exists on all scale-up levels, also called platform levels, i.e. lab, pilot, and production scale: Production scale exists on various levels with target scale of 0.1 to 1000 t/a of liquid or solid product. A pump type may change, when stepping to a larger scale, but the main characteristics must be compatible between the levels. On a certain platform level a PED with main equipment should offer a certain range of throughput, also called volume flexibility. Different flexibility of PEDs may exist for temperature, pressure, and chemical environment (mild for polymers and steel, aggressive for stainless steel, highly aggressive for special alloys or ceramics). Regulatory aspects may be important, such as ATEX or GMP requirements. Each aspect may become important, when considering higher throughput level with different environment. Prior scale-up, testing for the next larger platform level gives valuable information for critical parameters (e.g. mixing, heat transfer, residence time distribution, or separation performance). Testing is prepared and accompanied by process simulation with module analogues to evaluate operation windows and determine critical process parameters. Simulation with PED assists rapid process development and preparation of scale-up to the next platform level. Hence, PED also includes simulation models matching on different platform levels with different other ME. Scale-down of known equipment and process steps for lab suitability can be one option (lab analogues).

Table 3 presents a rough overview about **scale-up conditions** for important unit operations along with relevant parameters. For example, scale-up of micromixers concerns similar mixing characteristics, often observed with similar energy dissipation rate and measured by the pressure loss in the mixing device [14]. Heat transfer depends on the specific surface area (surface-to-volume ratio) and the flow rate, when keeping the logarithmic temperature difference constant. Further relations are given for chemical reactors with conversion and selectivity [24], separation units, and only sparsely for solids handling. Beside these scale-up guideline, parallelization of equipment as well as internal channel elements can serve for increase of volumetric throughput, also called numbering-up. The combination of scale-up by increasing equipment size and number has been shown as a very efficient measure for volatile market development [25].

Summing up, the following **key activities** are necessary for successful scale-up of ME:

- Operating companies together with academia and ME and PEA suppliers develop PEDs for a safe and reliable scale-up. They
  - model and handle exothermic reactions in a reliable way in relation with safety concerns.
  - model multiphase reactions including catalytic steps consistent on all length scales with dominant mass transfer.
  - develop downstream separation and purification processes to be available on laboratory and small- scale production scale for complete processes.
  - develop reliable solids handling in various process steps on all scale-up levels.

Confidence in lab scale modules gives the opportunity of skipping pilot plants and direct telescoping to production scale. Furthermore, novel business models may appear including rental equipment or special maintenance services, see Chapter 3.8.

3.5 Automation

The high process flexibility, as major benefit in modular plant design, requires a similar level of flexibility in process control systems as well as automation concepts to make use of the potential of Industry 4.0. The automation concept is critical to the aspired fast process adaption with low changeover times and reduced effort for plant operators. In addition to the control systems, data historians allow a remote access in order to perform data mining for process optimization and performance monitoring.

Modular Automation Concept

Already today, batch automation concepts allow hardware and control changes on a plant specific level by plant operators without (or with minimized) additional involvement of automation competencies, e.g. through reprogramming of process control system. Module intelligence paired with manufacturer independent diagnosis standards (e.g. NAMUR recommendation NE107) ensure effective lifecycle and service concepts via staggered remote diagnostics concepts. Staggered in this case implies reduced information for the operator and detailed information for maintenance. Modular automation with design of process units of high degree of intelligence and integrated control systems (black box module) with a super-ordinated orchestration is therefore the present key enabler for flexible plant operation.

Vertical and Horizontal Data Integration

Such autonomous, flexible control systems, which can already include model predictive control concepts based on physical or purely data driven models, are rarely realized at present. However, the vertical and horizontal data integration allows asset and process order management as well as process optimization.

The utilization of process data globally requires a decoupling from the process control area (e.g. via Unified Architecture, OPC-UA, as a gatekeeper), platform and hardware independent. This can be realized by data historian systems, which allow visualization of trends and the data export to other collaborative software systems.

Enabler for Tolerant Plant Operation and Performance Control

The process data is then available for analysis and can be combined with other information, e.g. from an ERP, PIM or MES system, to result in meaningful models which predict optimal performance and detect deviations. This type of performance control can be used to identify transient changes in the process itself, like fouling or catalyst aging, which lead to new target optima for control, ensuring tolerant plant operation. The data can be used in combination with information from the engineering of the plant (see chapter 3.7) to detect improvement potentials for plant design in the modular plant life cycle, e.g. debottlenecking. From these data mining activities, also an indication of missing sensors or the development of soft sensors for process control can be derived. However, the goal is to guarantee an automated and global access in cloud based server systems to realize vertical integration for plant management and horizontal integration for value chain optimization. A key element is the ensured safety in data transfer and authentication as well as know-how protection, where the support from IT (with Operational Technology “OT” expertise) is essential.

The mentioned examples emphasize the importance of manufacturer independent solutions as first step towards unified concepts within all hard- and software providers. Future exchange with NAMUR and ZVEI is necessary to evaluate standard interfaces in the area of automation and digital description of PEDs, based on e.g. module type package (NAMUR-MTP).

Summing up, the following **key activities** are necessary:

» Automation and process control suppliers as well as operating companies
  - apply super-ordinated orchestration of intelligent modules with manufacturer independent diagnosis standards to ensure flexibility in process control and module lifecycle concepts.
  - enable platform and hardware independent global access to process data decoupled from control area for remote diagnostics, process optimization and performance monitoring.
  - further develop novel sensor concepts to foster e.g. data mining activities and soft sensing.

3.6 Logistics and Supply Chain Management

Modular production concepts must be supported by modular logistics equipment and appropriate planning methods so that flexible production can leverage its potentials in practice. The planning of internal logistics, material flow and the layout or its reconfiguration on site should not take months or years of time, otherwise rapid development and reconfiguration of the production technology cannot be realized. A technical standardization of logistics equipment and the interfaces is also necessary for a quick start of production. Furthermore, it is important to make logistics equipment mobile and scalable, exactly in the same frame as specified by production. These requirements cannot be met by over-sized, fixed equipment. This leads to a variety of challenges for intralogistic issues. All include the common goal of creating reconfigurable, readily available plants, planning methods, and control systems for rapid implementation [8, 29].

Intralogistics

Modular production results in new challenges for the logistics processes of supply and disposal, in particular for the technical design and planning. Solutions are needed that define the logistics processes in autonomous functional units (e.g., storage, outgoing goods) and combine them to ensure their internal and external mobility and to be capable of reacting to the dynamics of production and market. To this end, logistical systems existing in industry and research are first analyzed for their scalability and their ability to be combined with reconfigurable production facilities and their mobility. This results in a **need for development** not only in means of **modularization** but also **intelligent equipment** which can be implemented in a plug and produce manner within Industry 4.0 environments [30].

In addition to the technical transfer into modular logistic systems, planning times must be shortened. Quick decisions to changes in the layout and for reconfiguring the site for an optimal material flow are necessary. New situations arise in a reconfigurable production whenever new plant modules are added or removed. An optimum material flow, from the view of flexible production and logistics modules, must be automated and fast. Therefore, **powerful assistant systems for (re)configuration of logistics setup** on site have to be developed. Placement and layout problems do not only exist site-specific, but also in the configuration of the production network with the newly gained degrees of freedom in terms of mobility and decentralization of a modular production [8].

Supply chain management and production network planning

Modular, decentralized production concepts open up new opportunities and possibilities with respect to supply chain management, choice of location and network structure. Mobility offers new degrees of freedom, especially with regard to customer orientation. A production located directly at the customer, production only on demand, a significant reduction in inventory, just-in-time production, and high delivery frequencies are only a few keywords in this regard. Also, a production on the site of the raw material providers and exploitation of local sources of raw materials offer attractiveness and potential savings, depending on the application scenario. Locally situated raw materials do not have to travel long distances to reach the production site, only to send back the subsequent product in return or further on.

Challenges in the production network mainly arise in the optimal site planning and production network design [31]. The **design of an economically optimal network with remote mobile assets** in contrast to production network planning in a conventional, large-scale, central production concept is much more complex and is further complicated by the fact that new market situations make dynamic adjustments to the network structure necessary. The **selection of sites, the number of equipment used and the allocation of customers to places of production** take place depending on the customer locations, the required amounts and the capacity of individual plants. Due to fluctuations in demand, both in time and space, all following states have to be planned dynamically. Adaptions in the network can take place, e.g. by relocation of plants, reallocation of customers to different sites or an increase or reduction of the number of PEFs at the site. High system dynamics and decision-making for the development of a variety of planning tools result in this complexity [31].

Summing up, the following **key activities** are necessary:

- Suppliers and academia develop modular, “intelligent“ equipment for material flow, storage and handling to support reconfigurable production equipment.
- Operating companies establish new logistic processes which allow for a fast (re)configuration of production and logistics.
- Operating companies, service providers and academia develop assistant systems for the (re)configuration of the logistics setup on the sites.
- Operating companies and academia create tools for a dynamic production network design.

3.7 Regulations

Regulatory requirements

Focus of this section is put on applications within the European Union. Nevertheless, some points and conclusions do not refer to any particular law field and others might be transferrable to other fields.

In European Union Law, any manufacturer has to declare that his product conforms to all legislative requirements. In the case of modular plants, the body (PEF) who is finally interconnecting PEAs and thus forming a new plant should declare the conformity. If the owner of the **plants changes** the configuration of its plant, i.e. change the sequence or combination of single PEAs, he should declare the conformity of the new configuration or assembling, respectively. As the freedom of creating new configurations is most likely one driving idea of modular plants, all owners should develop a procedure for ensuring and declaring the conformity. The “Blue Guide” on the implementation of EU product rules defines several different procedures for conformity assessments. Some of them would potentially allow simple assessment processes for modular plants if each single PEA were certified by the respective module supplier. In the opposite case, a conformity assessment would result in an excessive process, as the manufacturing part of the PEA would have been assessed retrospectively, e.g. by single unit tests.

Another challenge is to comply with national emission standards and environmental acts. The **national rules** might require a more or less detailed description of the plant, e.g. by providing P&IDs. Hence, if changes of the plant configuration go along with changes of the plant description or risk assessment, a **new authority approval** for operating the plant might be mandatory. For avoiding long lasting authority management processes, a sustainable approval strategy should be developed before the first set up of a modular plant, e.g. in cooperation with the local authorities. This strategy should provide a maximum of flexibility regarding configuration changes. A feasible strategy might be to develop a framework of possible configurations which are linked to particular (exemplary) processes.

Safety related functions would always be part of safety assessments. The idea of using only "intrinsically safe" PEAs will not always sufficiently meet all safety requirements. Risk assessments should always refer to the process and the necessity of realizing intermodular safety circuits will generally arise. Hence, the supplier of PEAs should be able to react on different safety strategies, e.g. providing an interface to digital safety protocols or terminal connections to analogue standard signals. It should be part of any safety strategy, to install only instruments of higher safety levels. On the other hand, the operator of modular plants should define his own general strategy of realizing safety related functions. The entire fleet of modules should comply with this strategy.

International regulations are not yet harmonized. The procedure to apply for permissions in the different law fields are varying between different countries. As one example there are regional standards for pressure vessels existing (Europe, USA, China, etc.). Currently it is not possible to transfer these vessels and therefore complete PEFs to another country without considering the different standards.

GMP ability

Operating modular plants in a GMP environment will face requirements which have to be defined prior to the design of the PEAs.

Requirements regarding conformity of materials such as steel and especially sealings are easy to fulfill, due to the fact that these compounds are already available on the market. Standard equipment such as pumps, valves, process sensors, etc. can also be purchased with an FDA approval. A **qualification** of the hardware built in one PEA following the FDA guidelines can be adopted from a standard batch equipment qualification.

The qualification of the PEA, which is running independently (state-based control), should be well prepared regarding the definition of parameters the PEA has to fulfill to ensure a process that can be validated. The **qualification framework** would be the PEA itself. The benefits would be an easy requalification when a PEA has to be changed for maintenance. An independent qualification of the PEA has to be the strategy to be prepared for a modular multi-purpose plant concept.

Validation of a process is focusing on the chemistry and interaction of the qualified PEAs. The strategy for a validation of a process in a modular multi-purpose plant is to validate the overall process including all PEAs needed to end up with a product which can be well characterized. All CPPs that define the CQAs have to be known and may be adopted from the conventional batch process if possible.

Introducing the modular plant concept for API production leads to special design of the piping and connection due to the important issue of cross contamination using the equipment as a multi-purpose plant. The new EU GMP guideline is discussing this issue and brings in examples on how to deal with limits of residues for a high potency modular production. **Cleaning concepts** will be a key topic for the design of PEDs. A vision of a small-scale continuous HPAPI (highly potent active pharmaceutical ingredient) production in small isolated containment can be possible with this flexible production concept.

An important step during the production of an API is the definition of a batch. Three strategies are thinkable to be followed: process time, product amount and amount of raw material. The quality by design initiative of the FDA compared with the concept of a modular plant fits to the strategy of the future pharma production.

Summing up, the following **key activities** are necessary:

- Authorities and operating companies
  - develop international standards, as they do not yet exist. The "Blue Guide" on the implementation of EU product rules would potentially allow simple assessment processes for modular plants, but a conformity assessment would turn out to an excessive process when it is done retrospectively.
  - adopt these regulations to easily comply with national emission standards and environmental acts in the field of modular plants.
- develop guidelines and workflows for the GMP ability of modular plants especially for special requirements such as cleaning, batch definition and validation.

3.8 New Business and Service Models

For the successful implementation of modular plant and production concepts, aside from the technical solutions, the development of appropriate business models will also be crucial. The business models will be different for the individual market parties and depend strongly on the industry (e.g. chemical specialties, pharma etc.) and on the role of different parties within the market (e.g. chemical company producing and selling chemical products or equipment / PEA supplier etc.).

The main parties on the market are

- Operating companies (chemical and pharmaceutical producers)
- Engineering companies
- Equipment suppliers
- Automation / process control suppliers

This is a simplified differentiation because the market parties can be different companies, but they can also partly or completely overlap (e.g. internal engineering departments in chemical companies vs. external engineering partners, internal workshops for construction of equipment and PEAs vs. external partners, but also many different combinations of external and internal competencies in investment projects).

For **operating companies** (chemical and pharmaceutical producers), a simple business model to gain profit with modularization is to continue producing and selling the same products. Modular plants offer a way to cheaper or quicker realization of investment projects and to invest stepwise over the years parallel to sales volume growth to maximize long term net present value (delayed investment) and to reduce the investment risk as each individual step then requires only minor or medium budget. This way the business model incorporates modular technologies to improve existing "conventional" businesses.

Another business model is local or decentralized production very close to the customer or even directly on customer's production sites. The benefit of such models can be reduction of logistics costs. Another driver could be the possibility to produce tailor-made products, which need to be adapted frequently to the applications of the customer. PEFs could also be completely integrated into the customer's production getting raw material from the customers, doing synthesis or physical modification inside the PEF and transferring the new/modified material back to customer's production process.

In this regard, additional potential can also be expected by using remote control technologies. This way, experts (e.g. in R&D) can assist in optimizing and trouble-shooting modules or implementing new recipes in a remote production site. To materialize such business models completely new methods of integration the internal work streams with the customers are necessary.

For **engineering companies** and **equipment suppliers** it could be a business model to provide ready to use PEDs and PEAs to chemical and pharmaceutical producers, which reduce their own engineering effort and can execute investment projects quicker and easier by just defining requirements for the modules. These PEAs are then designed and constructed in parallel by different engineering partners. Additionally the engineering companies can reduce their internal planning effort due to standardization and reuse of PEDs.

Another possibility of new business models could be for suppliers to also become a "producer", e.g. by leasing a PEA to the chemical/pharmaceutical producer and then providing services. The services can range from just a technical support to maintenance or even taking over the full operational responsibility for the PEA and selling product or a utility instead of selling process equipment or part of a chemical plant. Business models comprising elements of the ideas listed here do already exist, e.g. Linde provides plants for technical gases to their customers, but offers individualized service from technical support to full operation, too. For chemical production, however, comprising synthesis steps would be new, while many questions still need an answer. For **automation and process control suppliers** there are many new business opportunities associated with modularization, which are strongly related to Industry 4.0.

So far, business models are characterized as transaction orientated. This is due to change when modular production concepts emerge on the market, resulting in PEA manufacturers joining the market. If the chemical and pharmaceutical producers decide to use modular production concepts, the company will be confronted with new business models. A shift towards providers' (engineering companies and equipment suppliers as well as automation and process control suppliers) responsibilities and risk taking can be identified in this relationship. This is due to the modular production concept requiring different services in order to be attractive for chemical and pharmaceutical producers. The PEA manufacturer takes care of the plant over the entire life-cycle. Services such as remote control, apparatuses substitution or moving PEAs to different locations will emerge and will be necessary in order to gain the full potential of modular plants [32].

Summing up, the following **key activities** are necessary:

- All parties involved (operating companies, engineering companies, equipment suppliers and automation/process control suppliers as well as service providers) develop new business models, in which all main parties on the market can expect potential benefits in terms of revenue, costs and service.
- The mentioned parties clarify warranty, liability and conformity of production equipment.
- Suppliers develop module-lifecycle concepts including concepts for maintenance, repair and overhaul of production equipment.
- So far there is no market for modular plants and respective business models. Therefore, all parties create the willingness to support the modular approach.

4. Summary and Further Activities

Recent public funded projects successfully revealed the technical and economic potential of small to medium scale (0,1 – 1000 t/a) continuous production and demonstrated its technical feasibility in modular plants. Small scale continuous production addresses various business sectors such as specialties, fine chemicals, and pharmaceuticals manufacturing. Quick wins can be faster development times and resulting earlier time to market, savings in planning, engineering and purchasing effort, risk reduction and faster customer response times depending

Area	Key action points and fields of development	Key parties involved
Standardization and interfaces	» specification sheets for – common process and service PEDs – definition of interfaces	» Operating companies » Engineering companies » ME and PEA suppliers
Automation	» super-ordinated orchestration of intelligent modules with manufacturer independent diagnosis » platform and hardware independent global access » novel sensor concepts	» Automation and process control suppliers » Operating companies
Regulations	» international standards » adopting regulations to easily comply with national emission standards and environmental acts » guidelines and workflows for the GMP ability	» Authorities » Operating companies
Apparatus development	» new reactor geometries and designs, new materials and manufacturing approaches for reactors » new sensors for monitoring the reaction » compact equipment for downstream processes and for solid dosage » temperature management and heat insulation concepts » small scale, reliable equipment	» ME and PEA suppliers » Operating companies » Academia
Scale-up	» reliable modelling & handling exothermic reactions » modelling multiphase reactions including catalytic steps on all scales » downstream separation and purification processes on laboratory and small scale production scale » reliable solids handling in various process steps on all scale-up levels	» Operating companies » Academia » ME and PEA suppliers
Logistics and supply chain management	» modular, “intelligent“ intralogistic equipment » new logistics processes » assistant systems for (re)configuration on sites » tools for a dynamic production network design	» Logistic equipm. suppliers » Operating companies » Academia » Service providers
Planning process	» decision making in module based planning and design » prototypes of simulation decision support tools » new, robust design approaches » framework to implement the decision support tools	» Academia » Operating companies » Engineering software vendors
New business and service models	» new business models with benefits for all parties » warranty, liability and conformity » module-lifecycle concepts » willingness to support modular approach	» All parties mentioned

on the business case. However, further demand for development was found in the course of industrial demonstration. Required working areas and gaps in technology and planning methods exist in the areas of standardization and interfaces, automation, regulations, apparatus development, scale-up, logistics and supply chain management, planning process and new business and service models. These result in the following key action points and fields of development with the specified key parties involved.

In the view of the ProcessNet working group on modular plants these key action points and fields of development have the following priorities. Priorities have been set on basis of importance, field of resource investment and focus for the next 3-5 years.

Priority 1	essential precondition
Priority 2	ongoing activities to support modular approach
Priority 3	subsequent to priority 1 and/or priority 2 results

The areas of standardization and interfaces, automation as well as regulations are an essential precondition for modularization and therefore first priority. All of them have to start as soon as possible but they will include different time frames: Standardization and interfaces in the next three years (2017-2020), automation in the next five years (2017-2022) and regulations in the next ten years (2017-2027). The areas of apparatus development, scale-up and logistics and supply chain management are ongoing activities supporting the modular approach and therefore second priority. Planning processes and new business and service models depend on first or second priority results and are therefore subsequent to these and third priority. All key activities are initially mainly driven by the operating company but do depend on the interaction with the other mentioned respective key players.

Thus, the first of future activities of the ProcessNet working group are an interaction with the NAMUR on automation of modular plants, workshops with equipment suppliers and workshops with authorities. Aside from this, further activities include a prestage to a VDI guideline based on this white paper and an application of modular, continuous production to pharma and API production. The guideline activities will include further completions and details. The key action points are going to be tackled in public funded research projects like the ENPRO-initiative. Further joint research and development activities between industry and academia are necessary.

Glossary

2D:	two-dimensional
3D-CAD:	three-dimensional computer aided design
API:	active pharmaceutical ingredient
ATEX:	ATmosphères EXplosibles, explosive atmosphere
Big Data:	High volume data management and analysis
CapEx:	capital expenditure
CE:	EU conformity marking
Compatibility:	capacity of two or more systems for the exchange of information, materials, energy and media
CONSENS:	EU-funded research project, Integrated Control and Sensing
Continuous manufacturing:	chemical manufacturing in continuous-flow plant
CoPIRIDE:	EU-funded research project 2010-2013, Combining Process Intensification-driven Manufacture of Microstructured Reactors and Process Design
CPP:	critical process parameter
CQA:	critical quality attribute
CTQ:	critical to quality
DCS:	digital control system
DN:	nominal diameter
Downstream:	Work-up, separation and purification steps such as chromatography, crystallization, distillation, extraction, absorption etc.
DSP:	downstream processing
EcoTrainer:	container concepts as infrastructure for modular, small scale plants
Engineering phase:	conceptual, basic and detailed engineering
ENPRO initiative:	Energy Efficiency and Process Intensification for the Chemical Industry
ERP:	enterprise resource planning
EU:	European Union
EX:	see ATEX
F^3 Factory:	EU-funded research project 2010-2013, Fast-Flexible-Future
FDA:	Food and Drug Administration
Flexibility:	volume flow with different flow rates, process flow with different process conditions
GMP:	good manufacturing practice
HPAPI:	highly potent active pharmaceutical ingredient
Industry 4.0:	cyber-physical systems communicating in the Internet of things (IoT)
ISO container:	International Standardization Organization shipping container
IT:	Information technology
Lead time:	time span between product development and the fully operational plant
ME:	modular equipment
MES:	manufacturing execution system
MI:	modular infrastructure
Modularization:	Designing with standardized units, dimensions or interfaces, which can be easily assembled, maintained as well as flexibly arranged and operated; planning and construction with modules
Module:	functional process unit with standard dimensions and interfaces as well as connected databank with planning, construction, and operational information
MR-NMR:	medium resolution nuclear magnetic resonance spectroscopy

MTP:	module type package in automation
NAMUR:	User Association of Automation Technology in Process Industries
NCE:	new chemical entity
NE:	NAMUR recommendation
Numbering-up:	scale-up by parallel arrangement of equipment
OPC-UA:	open platform communication - unified architecture
OpEx:	operational expenditure
PAT:	process analytical technologies
PEA:	process equipment assembly, similar to module
PEC:	process equipment container, similar to 20-ft shipping container
PED:	process equipment design, module design, fabrication and operation information
PEF:	process equipment frame
PPD:	process plant design
P&ID:	pipe & instrumentation diagram
PIM:	process information management
Plug and produce:	Technology that allows an easy integration, removal or exchange of production equipment without the need of a specialist for the reconfiguration
R&D:	research and development
Scalability:	characteristic of a system to expand and increase its capacity
SWOT:	Strengths, Weaknesses, Opportunities, Threats
Time to market:	length of time from the first product idea to the finished product and its launch
Reconfigurable production:	adaptable, modular production concept including modularization, scalability, universality, compatibility and mobility
Reconfigurability:	see reconfigurable production
TRL:	technology readiness level
Upstream:	reaction technology, fermentation
USP:	upstream processing
ZVEI:	German Electrical and Electronic Manufacturers’ Association

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