pharmaceuticals: moving from experimentation to production

SUEZ

pharmaceuticals: moving from experimentation to production

Many pharmaceutical companies start out by manufacturing from a modest base, often working from a small business unit and then scaling-up their operations as demand grows or new product lines are taken on. This is also true for established manufacturers that are developing new products, as they will start from a low base, using small-scale laboratory testing before bringing new pharmaceuticals to market.

From a "benchtop" or laboratory operation, a successful pharmaceuticals enterprise can soon migrate to a pre-production pilot plant and then ultimately on to high volume production.

However, the process of scaling-up from low to high volume production is not always a simple task and requires a clear understanding of the critical phases involved – as well as ways to keep these under control as volumes change.

There are many issues to consider, including:

- Possible changes in product characteristics when increasing batch sizes
- The question of batch production or continuous processing
- Subsequent equipment requirements
- Energy usage
- Level of automation
- Consistent quality control
- Validation
- Compliance with regulatory standards
- Profitability

In each case, it should be recognised that successful implementation depends on the input from many areas of the business, from product development, production, QA and management teams as well as external assistance and advice from experts in the field of water purification.

Documents offering advice on up-scaling production usually centre on the constituent that is the most abundant in the majority of pharmaceutical formulations; that constituent being typically referred to as "Aqua" or (purified water).

Scaling-up your water purification requirements
From the perspective of water purification, moving from low volume laboratory trials through to batch or full production should not be a complex process. The key consideration is that the inherent nature of the product being manufactured remains unchanged as does the quality of purified water required to produce it.

pharmaceuticals: moving from experimentation to production

Step by step approach

The first step would be to commission the drafting up of a document typically referred to as a (URS) or User Requirements Specification. The (URS) typically scopes out and defines the requirements of the water purification system. It should be detailed enough to provide sufficient information to allow any water purification system provider to propose a working solution to meet the requirements necessary to provide purified water at the specified quality, quantity, consistently; day in, day out.

To assist you at this stage you may wish to employ the services of an external water purification expert or company such as SUEZ to carry out an audit and site survey of your existing water system and future purified water demands.

As part of the audit SUEZ can advise on achieving the relevant water quality standards, providing consultation and expert advice that will help you negotiate the maze of validation requirements faced when drawing up a water treatment solution. Crucially, SUEZ will advise you on how to move into batch production while minimising the likelihood of revalidation should you move to volume production.

The first stage of the water audit would typically involve the taking of representative samples of your incoming feedwater supply for detailed mineral and microbiological analysis.

This information may already be available from your local authority or water supplier if you are using a mains supply but should nonetheless be checked; if a surface water or borehole source is being used then a detailed analysis of water characteristics is crucial.

An evaluation of the pre-treatment system can be made and a specification be drawn up. If water conditions are variable, then the design of raw water treatment systems and the provision of pre-treatment will need to be suitable for worst case conditions.

At the end of this document is a typical checklist which can be used, as a guide, to capture all the key parameters to be considered when making the move from experimentation to production.

The next stage would be to evaluate the necessary size of the water purification units and again your water purification provider will guide you through this process. Calculating the maximum demand and also establishing the volume needed on a regular basis will ensure that

pharmaceuticals: moving from experimentation to production

any immediate and forthcoming needs are catered for and prevent any unnecessary expense further down the line that may be incurred by altering the design and necessitating revalidation.

The method by which pure water is drawn into the process must also be considered. For example, if supplies are required at different locations a centralised system feeding a ring-main may be more appropriate, offering an unobtrusive and space-saving option that can deliver high volumes and high quality. In centralised systems, it may be possible to make gains in efficiency if pumps are linked to variable speed drives, enabling the speed of each pump to be matched exactly to the output demands of the process and water treatment system.

Providing the right capacity can also mean that storage has to be part of the solution. Some water purification systems for pharmaceutical manufacture are designed to take potable feed water directly from the mains, purify it using Reverse Osmosis (RO) technology, store it in an integral storage tank, and circulate it via a ring main to multiple points.

Depending on the application, higher volume production operations essentially use scaled up versions of the smaller water purification systems, perhaps supplemented by systems such as: sand and multi-media filters, for eliminating particulates; activated carbon adsorption systems for the removal of organic contaminants and chlorine compounds that can affect colour, taste and odour; cartridge filtration, for pre-treatment; and reverse osmosis for the removal of ionic contaminants. In addition, ion exchange technology is often used to soften and deionise water, with UV irradiation and membrane filtration commonly being added to maintain microbiological integrity.

Reverse osmosis (RO) is one of the most commonly used technologies and incorporates specialised semi-permeable membranes through which pressurised feed water is passed to remove inorganic ions and dissolved organic contaminants. This process enables up to 98% of the dissolved minerals and salts contained in the raw water supply to be rejected, together with silica, organic compounds and bacteria; typically, over 99% of micro-organisms can be eliminated.

Once the water side of the audit has been completed consideration should be made as to the operation and functionality of the intended equipment. Within the (URS) document a section relating to "System Definition" may include for example, details as to the preferred Functionality, Operating Regime, Process & Product

pharmaceuticals: moving from experimentation to production

Parameters, Materials of Construction and Operating Environment etc.... For example, the "Operating regime" may specify that the water purification unit and storage tank must be housed within a pre-built dedicated room constructed to maintain a clean operating environment and easy access to equipment and controls.

Once you have considered all of these areas you will then be in a much stronger and clearer position to create a small final 'model' of what will be the larger system. The next stage will be to select a suitable partner to deliver your requirements. Choose a supplier you trust, has a proven track record and who you can work with; the best supplier is unlikely to be the one with the cheapest unit price for the system but one you feel you can work with and which can provide ongoing expertise and support. Trials and validation for pharmaceuticals may take years and revalidation as a result of changes made to your process are expensive; the most cost-effective way to specify equipment and produce pharmaceuticals that maximise revenue is therefore to work with a provider that can supply the most appropriate equipment and that understands your needs both now and in the future.

Please contact us to discuss your applications or start up requirements. Our advice is free of charge, and we will be happy to undertake free site surveys if required.

More information on water purification specification can be found at: www.purite.com

Moving from experimentation to production

Below is a list of the key considerations when making the move from experimentation to production and compiling an initial (URS) document:

- On-site contact details
- Brief description of process
- Treated water quality requirements
- Water demand/usage
- Feed water analysis
- Specific system requirements:
    - Materials of construction
    - Methods of sanitisation
    - Storage requirements, etc.
- Distribution
    - i.e. Ring Main Lengths/material
- Controls and functionality
- Validation

the process of scaling-up from low to high volume production is not always a simple task and requires a clear understanding of the critical phases involved

Contact

Water Purification Systems

Email: mail.waterpurificationsystems.uk@suez.com

Web: www.suezwatertechnologies.com