Are You Using the Correct Grade of Raw Materials to Minimize Risk, Increase Product Integrity?

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The need to comply with continually evolving regulatory requirements is placing an increasing strain on drug manufacturers. As they work to create new and effective drugs that adhere to these strict requirements, manufacturers have become more reliant on their raw material suppliers to ensure product compliance. It is paramount for them to find a supplier that not only meets the necessary regulations, but understands the way these requirements expand as a drug moves through the development process.

Each individual company involved in the research, development, testing, and commercial manufacture of pharmaceutical products represents an important step in the process and affects the overall integrity of the supply chain.

An Expensive Process

Drug manufacturers invest a great amount of time and money in the research and development of new medicines. On average, the process from the discovery of a promising molecule (lead compound) to a marketable drug approved by regulatory authorities around the world, may take up to 15 years. Only one in 10,000 potential drug candidates may ever reach the pharmacy, and only one out of three of these drugs may ultimately recoup its initial development costs.

During the scale-up phase of a product’s development, many companies find themselves in a situation where regulatory requirements for raw materials are less specific, and guidelines are more open to interpretation. Most companies will focus on reducing risk in their products by pursuing supply chain transparency, change management and extensive documentation. They may be willing to use non-critical raw materials that have consistency and control, but do not necessarily meet the same GMP (Good Manufacturing Practice) standards required of final drug products.

This approach changes as a company moves through the pipeline from research to commercialization, when the materials they use become subject to a grading system that defines whether they are compliant with industry regulations. This often means moving to a customized raw material rather than one that is available off the shelf.

Quality from the Start

As a product moves from lab scale research and development through each phase along the way to commercialization, the guarantee of no contamination becomes ever more crucial. Any lower grade or non-pharmaceutical grade substances used in manufacturing run the risk of containing undefined and/or higher levels of contaminants which could introduce unwanted experimental variables. This could have detrimental effects on the drug development process, and highlights the need for manufacturers to find the right balance between cost and quality.

When seeking this balance, the hardest decision for a drug manufacturer can often be choosing the level of quality to implement in the earlier stages of research and development, before the product reaches clinical trials. Using quality raw materials from the start not only ensures that you have the right ingredients with all the necessary regulatory back up, but it can also bring significant advantages from a cost and supply chain perspective. It also guarantees that, once the product moves forward into clinical trials, it will be backed by full transparency documentation, certificates of origin for raw materials and a secure supply chain with integrity.

The Stops Along the Way...

Each step of the drug development process brings greater responsibility to the manufacturer. If the product development process is approached in the correct fashion, by the time a product hits Phase III, it should be prepped to go commercial, once all the trials demanded by the regulators have been completed and it is given marketing authorization.

In the early stages of clinical trials – Phase I safety trials and Phase II proof-of-concept trials – the primary requirement is to make sufficient quantities of the investigational drug to meet trial...
needs. When it moves on to the large-scale Phase III trials, the key factor is the ability to transition from small-scale clinical to large-scale commercial manufacturing. This is often the point where a manufacturer will switch the clinical batch manufacturing process from liquid to powdered media, and lock down any remaining regulatory aspects of the commercial manufacturing process.

Once the drug is approved, it becomes available to patients, with on-going Phase IV monitoring for unforeseen side-effects that only become apparent when it is used in much larger patient populations. On the manufacturing side, the focus shifts to supply chain management and timely delivery, focusing on improving the yield, CAPA (corrective and preventative action) plan development and managing key suppliers. The biggest concerns include changing formulations and/or dose regimens, for example developing extended release formulations, and applying for label extensions to enable the drug to be prescribed for additional indications.

**What to Look for from a Supplier**

Raw materials sourced for use in commercial products must be manufactured in a way that meets the requirements of the biopharmaceutical regulated manufacturing process. Drug manufacturers should look to work with a supplier that offers classified products, from non-regulated, non-GMP raw materials to highly regulated GMP products; the breadth of offering will serve to ease transitions through each development phase.

When seeking a supplier, it is important to verify that they offer an optimized supply chain and issue resolution, as well as being able to help develop risk mitigation strategies and even look to provide assistance with shortening timelines in development programs. Other important factors include:

**Process Control** – Qualified suppliers will have top-of-the-line facilities that are equipped with the latest technologies. This allows them to manufacture quality products consistently that are reliably free of contaminants. Additionally, this allows the supplier to offer clear documentation for each product, to ensure full disclosure to the client.

**Regulatory Support** – With an increasingly strict regulatory environment, and one that can vary geographically, it is imperative that a supplier understands the regulations, and also works to stay updated on any new developments. In other words, the supplier should stay ahead of the regulations so manufacturers are not burdened with the lengthy research that would otherwise be needed to ensure full regulatory compliance for each step of the development process.

**Supply Chain Information** – It is not enough to simply have a strong supply chain. A good supplier will be able to validate this supply chain with full documentation and transparency to ensure access to the ingredients as soon as they are needed. The supplier should provide guidelines on the appropriate quality level for each application, and provide an understanding of the implications of that decision.

**Supply Chain Control** – In an increasingly global market, being able to access supplies of necessary raw materials, and having a fall back for where they come from, is crucial. A secured supply chain, with redundant facilities in different locations, allows a supplier to guarantee the availability of its products, even when disaster strikes. In addition, it is imperative that a supplier has a change control notification program to keep customers constantly informed of any changes in the raw materials supply.

**SAFC’s Approach**

SAFC, a member of the Sigma-Aldrich family, is dedicated to solving manufacturing challenges by providing customers with tailored quality and regulatory support for product applications. SAFC classifies the majority of the Sigma-Aldrich products under one of the four levels of the Enhanced Quality Program, from the non-regulated, non-GMP raw materials to highly-regulated GMP products.

Each level has associated quality support and documentation, along with recommended use and change notification parameters. By differentiating the products, SAFC helps take the guesswork out of the process. The PharmaGrade products provide clearly defined and classified raw materials for use in development.

Regardless of the tier of product sourced, SAFC is able to offer support throughout development. From the ability to offer products as readily available inventory to maximize time, to offering scientists, researchers and manufacturing specialists whom are able to provide insight into the appropriate grade of raw materials for each step, SAFC is capable of providing the resources needed along the way. All of this is further supported by the appropriate documentation, required by the regulators, that corresponds to the specified manufacturing requirements in each stage – from discovery to development and from clinical trials to commercialization.

Encompassing a dynamic product list of raw materials, supplements, buffers, enzymes and other products used in biopharmaceutical, pharmaceutical and diagnostic applications, SAFC has the capabilities to match the appropriate level of service that a manufacturer’s risk mitigation needs call for.

To learn more about SAFC’s Enhanced Quality Program, please visit: safcglobal.com/enhancedquality

To learn more about SAFC’s high quality product line, PharmaGrade, please visit: safcglobal.com/pharmagrade