High-functionality co-processed excipients enable continuous processing.

Selecting the proper excipients is critical to the success of any tablet formulation. To assist formulators in selecting excipients and overcoming tablet formulation challenges, JRS Pharma has created a *Tablet Formulation Guide*. The guide provides detailed direction regarding excipient selection and suggestions for suitable formulation approaches. *Pharmaceutical Technology* recently spoke with Michael Nagel, Scientist III, R&D at JRS Pharma, about how the *Tablet Formulation Guide* can be a critical tool to decrease preliminary formulation development time.

**Pharmaceutical Technology:** How does the *Tablet Formulation Guide* assist formulation development?

**Nagel:** Selecting the proper excipients is critical to the success of any formulation. JRS's guide focuses on excipient selection and assists the formulator in overcoming formulation challenges. The *Tablet Formulation Guide* takes into account numerous aspects of the API, including dose level, flowability, compactibility, and solubility in order to provide suggestions on a variety of commonly available excipients as well as a recommended process to overcome potential formulation challenges. API formulation examples are also provided. The *Tablet Formulation Guide* can be a critical tool to the formulator to decrease the time needed to develop a preliminary formulation.

**Pharmaceutical Technology:** Why does the *Tablet Formulation Guide* recommend using high-functionality co-processed excipients in challenging formulations?

**Nagel:** The majority of new APIs in development are low-dose, poorly soluble drugs. As a result, they are typically micronized and are cohesive in nature. This creates challenges for the formulator and for the excipients.

The formulator has to select a process that is compatible with the API from a stability perspective and also provides enough energy in the process. This may include high shear mixing or even a milling step to break up and disperse the agglomerates of the cohesive drug within the mixture of excipients in the formulation to create a uniform blend.

The excipients, on the other hand, must promote blending by reducing the cohesive nature of the API while providing good flow and compatibility with the final blend, resulting in a robust...
tablet that has the desired performance characteristics. For these requirements, high-functionality co-processed excipients give the best performance.

**Pharmaceutical Technology:** Why do the terms high-functionality and co-processed go hand in hand?  
**Nagel:** Co-processed excipients were developed to provide more than one functionality in one formulation component rather than using two or more components separately to gain the benefits of their individual functionalities. For example, one component excipient may provide good flow while another may provide good compaction, thus requiring the use of both to gain benefits from each. Co-processed excipients composed of both components may have the enhanced functionality of both parts in one composite material, making it a high-functionality co-processed excipient.

**Pharmaceutical Technology:** Why does the Tablet Formulation Guide recommend two choices for lubricants as well as specific instances where one is recommended and the other is not?  
**Nagel:** The most widely used lubricant is magnesium stearate. While effective, it has some drawbacks and incompatibilities that can lead to formulation challenges, product performance failures, and, in extreme cases, batch failures. Magnesium stearate also can significantly reduce the compactibility of a blend and impair or even prevent the dissolution of the API in a formulation if it is used at too high a level or is over-mixed. In many applications, we recommend the use of magnesium stearate, but it must be used carefully to avoid these issues.

In more critical applications, in which a poorly soluble and/or less compatible API is used, we recommend using sodium stearyl fumarate. This is a high-performance lubricant that has fewer incompatibilities with drug compounds and has a much lower impact on the compactibility of the blend and dissolution characteristics of the finished product. Using sodium stearyl fumarate can avoid the problems and potential batch failures associated with magnesium stearate.

**Pharmaceutical Technology:** Will the use of high-functionality co-processed excipients and this high-performance lubricant come with a hefty price increase to the finished product?  
**Nagel:** That is a common concern and is one that has sadly led to many costly, but avoidable product problems. When one considers the cost that excipients impart on the total costs associated with manufacturing of the finished drug product (approximately 2%), the added cost of using better excipients is minimal. Many people only look at the cost difference between conventional excipients and high-functionality excipients and do not think about the costs associated with one potential downstream production problem or batch failure.

In a batch failure situation, the excipient costs are miniscule in comparison with the costs of lost API, materials, manufacturing time, human resource time, cleaning, QA investigations, and product destruction. If the scenario involves a controlled substance, there are losses in allotment quota that the manufacturer is granted by the DEA. Using high-functionality excipients is cheap insurance.

**Pharmaceutical Technology:** Are there any other benefits or applications of high-functionality co-processed excipients in pharma manufacturing?  
**Nagel:** High-functionality co-processed excipients provide benefits in continuous processing because of their enhanced blending, compactibility and benefits to finished product integrity. Co-processed excipients typically contain two or more formulation components that address several finished product needs. For example, one co-processed excipient, JRS’s PROSOLV® EASYtab, contains a binder to provide bulk and tablet toughness, a disintegrant to promote tablet disintegration, a glidant to enhance blending and flowability during processing, and a lubricant to aid in the tableting process.

Co-processed excipient can provide these individual components in the needed ratios as a ready-to-use composite product that can be fed into a continuous process through one feeding device. If these components were used as four separate conventional excipients, they would have to be fed into the process using four separate feeding devices, requiring four times the monitoring and control to achieve the same composition without the same performance benefits of high functionality. Co-processed excipients are the excipients of the future.

JRS Pharma manufactures a complete portfolio of excipients and offers technical support and biopharma services to address formulation challenges. A copy of the JRS Tablet Formulation Guide will be available on the JRS website or a copy can be requested by emailing info@JRSpharma.com.