The pharmaceutical industry has devoted much effort to create new, complex, novel dosage forms in a quest to find easier, more reliable ways to administer medication to patients. The quest to improve patient experience on the journey to an improved quality of life has been noble. But it doesn’t have to be this complex. There is one novel dosage form that has withstood the test of time and stands apart from other novel dosage forms – suppositories.

A suppository is a dosage form that is inserted into the rectum (rectal suppository), vagina (vaginal suppository) or urethra (urethral suppository), where it dissolves or melts and is absorbed into the blood stream. Suppositories can deliver both systemically and locally acting medications and are a simple, proven way to effectively deliver medicine. Its most prevalent use is in Europe and Japan.

Traditional dosage forms such as tablets, capsules, and syrups are often convenient and effective, however, they present challenges for some patients. For patients with a vomiting tendency, these oral medications can be vomited out, reducing or altogether eliminating the intended benefit. Similarly, drugs prone to causing stomach upset are often better tolerated in suppository form.

Increased demand for suppositories as a dosage form presents a tangible opportunity for pharmaceutical companies today. As a large portion of the US population ages in the coming decades, there is enormous potential in this largely untapped market. A 2014 study found that “by offering an active ingredient solely as a tablet or capsule, pharmaceutical and life sciences companies ignore the needs of more than 50% of their target audience …”

This paper examines the suppository dosage form, challenges with traditional dosage forms, the coming increase in global demand, and finally, questions to ask when choosing a reliable partner for development and manufacturing.

ARE TRADITIONAL DOSAGE FORMS LESS EFFECTIVE?
The short answer is – sometimes. Although the oral route is considered the simplest and often most cost-efficient way of drug delivery, consumer demands
are changing. Likewise, other challenges arise ranging from patient symptoms, lack of access, lack of proper storage, and according to a recent survey, increased swallowing problems within the general population.

For some diseases, like severe malaria, the risk of death is largely dependent on the time lag between the onset of symptoms and treatment. Immediate access to effective treatment is critical to survival. For many patients, readily available oral drugs cannot be taken because of their symptoms, e.g., vomiting, convulsions, coma, etc. Hospitals that could provide alternative, non-oral treatments are often inaccessible.

One effective solution to treating severe malaria disease has been suppositories – which can be made available in remote areas and given at the onset of symptoms. A major clinical trial published in 2009 found that “if patients with severe malaria cannot be treated orally and access to injections will take several hours, a single inexpensive artesunate suppository at the time of referral substantially reduces the risk of death or permanent disability.”

Another case where traditional dosage forms were ineffective arose during the recent H1N1 influenza pandemic. Patients were unable to swallow traditional dosage forms due to acute nausea. Alarmingly, patients at the highest risk for the influenza virus (infants and the elderly) were found uncooperative with oral dosage forms. This made it difficult to assess whether the correct dose was actually taken by those most at risk. According to two small studies, a suppository of interferon alpha-2b, vitamin C, and vitamin E was developed and performed as well as the dominant oral treatment.

The two situations above are examples of seasonality or locale playing a role in market demand for suppositories. There is a larger, more stable opportunity, that is, not dependent upon pandemics or geography.

A recent study, titled “A Hard Truth to Swallow,” sought to explore the nature of difficulties in swallowing tablets and the impact on patients. The study was designed to reflect overall population demographics in age, gender and ethnicity. It found that conventional tablets and capsules come with a range of drawbacks and may no longer be the best solution for large segments of the population.

Key findings showed more than 55% of people, regardless of age or gender, experience “swallowing difficulties when taking tablets or capsules.” Though 44% of participants 65 years or older were affected, 70% of younger people, aged 16–34 also reported this problem. A wide variety of reasons were cited, but the most frequent were related to tablets or capsules being too large to swallow, becoming stuck in the throat and having an unpleasant taste or odor.

Moreover, swallowing difficulties are likely to negatively affect patient compliance with medications. Study participants resorted to modifying the medication in a variety of ways, the two most common being:

- Breaking tablets before ingesting them
- Crushing pills and dissolving in water

Both of these can affect API release profile, bioavailability and medical efficacy. Even more alarming, 8% resorted to not taking their medication at all.

This enormous market – patients in the first world who report significant difficulty with swallowing – anxiously awaits a solution that will be both effective and improve patient experience.

**FINDING THE RIGHT PARTNER**
Designing dosage forms to target different cultures, ages and preferences aims to better meet the needs of specific patient populations. By creating user-friendly
dosage forms, a company can differentiate itself from the competition. This approach yields other benefits, mainly, ability to expand existing product lines, prolong product lifecycles, breed customer loyalty and at the same time increase revenues.

There are just a handful of suppository contract manufacturers operating in North America — so, there is competition. As you consider the right partner, ask them about their experience and capability in the following key areas:

1. **Formulation** — Does the partner have experience making suppositories using a variety of bases, e.g. cocoa butter and semi-synthetic hard fats? What is their experience with suspensions, which present a uniformity challenge in manufacturing and filling? Can they manufacture suppositories containing narcotic and controlled substances?

2. **Raw materials** — Does the partner accept raw materials from clients? Do they have ability to assist you in sourcing raw materials?

3. **Filling** — Does the partner specialize in aluminum composite foil, the preferred packaging method (protects active ingredients from light exposure while providing superior vapor and oxygen barrier)?

4. **Production at scale** — Is the partner able to scale up or down with batch sizes?

5. **Global capability** — Does the partner have experience delivering globally? Do they have temperature and humidity controlled warehouses? Do they have the ability to handle and ship temperature sensitive raw materials and finished products?

6. **Tech Transfer** — Does the partner have on site analytical labs? Can they easily develop and transfer analytical methods to support future commercial operations? Can they take your currently marketed product and transfer the manufacturing process to their site for outsourced manufacturing?

Confab delivers on each of these. With experience developing and manufacturing products for dozens of clients delivering to US, Canadian, European, and Asian markets. Once you’ve compared us to other potential partners, you’ll see that Confab stands alone in its ability to deliver a complete suite of development, manufacturing, sourcing and distribution services.

Confab’s expertise in developing and manufacturing suppositories is well earned. With over 20 years’ experience with suppositories, we have solved countless formulation and dosage form challenges. We can save you time and money in your development and manufacturing efforts. As the saying goes, you can “pay now, or pay later.” Any perceived savings of time and money in the near term can be lost if you don’t select the right partner. An inexperienced partner learns as you learn. Their mistakes become your mistakes. The cost is measured in time, money, and lost opportunity.
CONCLUSION
As discussed above, the suppository has gained popularity as a dosage form to best address a variety of challenges with the delivery of medicine. In some cases, a patient’s remote location prevents access to a hospital that could provide alternative, non-oral treatment. Other times a patient’s symptoms prevents effective delivery of an oral dosage form, due to vomiting, convulsions, coma, etc. Recent evidence points to an increased difficulty in swallowing for a large segment of the general population. In each of these cases, the suppository dosage form can and has provided a solution.

One major benefit of suppositories is the rapid absorption of the drug from the drug product. Highly vascularized mucosal membranes enable absorption of the drug product while bypassing the hepatic system, causing patients to experience faster onset, higher bioavailability, shorter peak, and shorter duration than an equivalent oral dose.

The largest market opportunity for suppositories today is identified in a 2014 survey which indicates over 50% of patients in the first world report significant difficulty with swallowing. In particular two segments of the population suffer more from this difficulty – those over 65 years of age and a younger group, aged 16 – 34 years.

As with the development and manufacturing of all drug products, regulatory agencies continue to demand that drug companies demonstrate deep understanding of their drug’s formulation, performance, and consistency. When you partner with Confab, you get ready access to complete development services including validated stability testing, process and cleaning validation, providing for a total and complete submission package.

Additionally, our manufacturing capability is unparalleled. We can deliver at massive scale including the manufacture of suppositories that contain narcotics and/or controlled substances. Our relationships with global suppliers and distribution channels allow us to safely ship your drug product across the globe.

When it comes to developing and manufacturing semi-solids, Confab offers expertise that simplifies the complexities of suppository development and manufacturing.

To discuss your suppository needs and how Confab can help, contact us at www.Confab.com or call 1-888-826-6322.

ABOUT CONFAB
Confab, a DPT Company, is a contract development and manufacturing organization (CDMO) helping pharmaceutical companies achieve clinical and commercial success. Our experts are focused on providing the answers you need from development through commercialization. We bring vast experience in resolving challenges in semi-solids & liquids and solid dosage forms. Our cGMP facility located in Saint-Hubert, Québec offers full-service outsourcing solutions including stand-alone development, site transfers, state-of-the-art manufacturing, packaging, and worldwide distribution.