



ADVANCING PATIENT-CENTRIC PARENTERAL DRUG STRATEGIES

→ BY **MARGA VIÑES** AND **ORIOI PRAT**, GRIFOLS

Parenterally administered drugs will remain the delivery option of choice, especially in the era of biologics, but their ultimate success therapeutically and commercially hinges on how well these drugs can be integrated into a patient-centric continuum of care.

For the foreseeable future, therapies delivered via parenteral routes will dominate advancements in healthcare and patient outcomes. Regulators, governments, health systems and – most importantly – patients are all stakeholders, linked by dependence on the safe, reliable and abundant supply of sterile liquid drugs. There is little dispute that this sector of pharmacopeia represents a tremendous growing opportunity for drug innovators and owners. But bringing a parenteral product to market successfully, then sustaining its long-term commercial and therapeutic success, is extremely challenging, requiring a broad and all-encompassing strategy well integrated into the patient-centric continuum of care. Industry leaders are very deliberately pursuing these strategies, but increasingly not without involving the intense and strategic collaboration of contract manufacturing and development organizations.

Not widely available until the 1950s, intravenously (IV) administered medications have become a central feature of modern healthcare. Most major categories of biopharmaceuticals and biologics – and most vaccines, antibiotics, immunotherapies and similar therapeutic IV-delivered substances like plasma and saline – are parenterals. Spanning the continuum of care, parenterals are delivered to caregivers and patients in a broad array of primary packaging and administration regimes. Primary packaging and dosage forms are also following major patient-centric trends, and innovation here is introducing new complexities for both manufacturers and consumers.

INFUSION OR INJECTION?

Intravenous infusion is the most common parenteral delivery method, providing an immediate therapeutic effect by delivering medication directly into the bloodstream. Small-volume parenterals (less than 100 mL) and large-volume parenterals (100 mL or greater) are both specified by the millions for the continuous or intermittent infusion of drugs and therapeutic fluids. Caregivers and patients encounter these forms across the continuum of care.

Admixtures are generally dried and most often lyophilized drug products pack-

aged primarily in glass vials or ampoules. In the case of many large-molecule drugs, including antibiotics, a lyophilized admixture of the drug is reconstituted and placed into an IV solution by a nurse or by a compounding pharmacist or some other medical personnel. When added into solution in this manner, the margin for human error looms large. It's not surprising that with admixture-based dosing regimens, the opportunity for error is present throughout all stages of the process – from preparation and dose calculation through to infusion. Intrinsically error-prone already, many healthcare systems access IV therapies through compounding pharmacies, which have generated a significant history of medical error introduced in the admixture formulation process.

In a 2001 report, a five-year FDA study found that the most common medical errors resulting in patient death were administering an improper dose (40.9%).¹ These errors can be exacerbated in a situation where multiple steps, like administering admixtures, is required. The more complicated the solution, the greater the margin for error. In 2010, a six-week-old infant died because a PN solution the infant was receiving had 60 times the amount of sodium than was supposed to have been prescribed. In 2007, a preterm infant received a 1,000-fold overdose of zinc, which was entered incorrectly into an automated PN compounder – a total of six staff members missed it.¹

Compounded admixture IVs were not primarily regulated by the FDA because they are generally customized combinations of already-approved drugs. The FDA had ordinarily given oversight authority to state pharmaceutical boards, but who can forget the October 2012 incident involving a compounding pharmacy in Massachusetts releasing 17,000 vials contaminated with meningitis that subsequently caused several patient deaths? Incidents caused by unsafe or unsanitary practices in the making and distributing of parenterals or custom IVs – by outsourced compounding agencies or by in-house compounding pharmacies – led to the FDA's passing of the Compounding Quality Act that regulates those agencies outsourcing medicines.²

Complicated admixture procedure was

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at the heart of it. The Institute for Safe Medication Practices 2009 study "The State of Pharmacy Compounding Survey" found that 30% of hospitals had experienced a patient event attributed to an admixture-related compounding error over a period of five years. Among the study's conclusions: the use of premixed IV solutions could have reduced such life-threatening or damaging incidents.^{3,4}

GREAT RISK, GREAT REWARD

The world's major health systems and drug-developing leaders are spending billions to help bring new (or high-demand or supply-challenged) injectable and infusible therapeutics to the market. The demand for premixed solutions is also therapeutically led. Premixed IV solutions, for example, are the preferred mode of delivery for antibiotics globally and a market segment growing exponentially. According to one study, the world's consumption of antibiotics has risen ~36% since 2000.⁵ Pain management and cardiac medications (both very popular therapeutic categories) are most often delivered intravenously, contributing to the demand for a safer, more reliable premixed solution.

To support these initiatives, drug owners are prompted to adapt their business models and frame them to meet the realities and risks associated with parenteral drugs. For an increasing number of companies, seeking technically and operationally superior contract-service partners to deliver capacity and resources is becoming a key component of their patient-centric strategy and the fastest path to market.

Overall design of the premixed fill, package material, and the functional attributes of the IV bag are integral to patient-centric

GRIFOLS:

Types Of Containers

Grifols Partnership is specialized in developing and manufacturing high-quality sterile solutions and lipid emulsions in a wide range of containers made from a variety of materials in different sizes to suit every need in both the human and veterinary markets.

Glass bottle: Naturally inert material, totally transparent and recyclable. Available sizes: 100 mL, 250 mL and 500 mL.

Glass vials: Available sizes 5ml to 50ml.

Polypropylene bag: Totally PVC-free. Excellent drug compatibility, very flexible and transparent material. Available sizes: 100 mL, 250 mL, 500 ml and 1000 mL.

product strategies. Grifols, which has a 75-year history developing plasma-derived medicines, provides a knowledge base and a source for design wisdom to create par-

enteral vessels intended to support successful healthcare and patient outcomes.

Plastic primary packaging for parenterals has been supplanting glass for decades and its positive attributes regarding pharmaceutical delivery and aseptic process benefits are well documented. Packaged in flexible bags, Grifols Partnership premixed solutions deliver a fixed dose in 50 mL to 1 L containers. These bags are terminally sterilized to assure sterility and safety. It is this specific dose feature that guarantees the patient receives an accurate dose while eliminating the potential for waste. Another example of the benefits of premixture versus admixture delivery strategies is that reasonable dosage limits are likely to encourage healthcare providers to write more cost-effective orders. Another advantage of premix bags involves shelf life and logistical capabilities – admixtures must be used between 24 and 48 hours – whereas premixed formulations can have a shelf life as long as two years.

GRIFOLS PARTNERSHIP PARENTERAL STRATEGY LEADER

It is well established that parenteral drugs and therapeutic fluids require highly controlled, sterile process environments to be manufactured correctly and to current GMP standards. Processing parenteral drugs is extremely challenging and any re-

view of drug recalls over the past 10 years will confirm this. Safety and quality in aseptic processing requires a tremendous focus on both process and understanding of process technologies, as well as an extremely well-integrated and -aligned quality system backing it up.

It is a complex and costly undertaking to advance a parenteral drug product. To achieve market and therapeutic success, a range of specific requirements is mandatory. This includes category expertise, integrated and aligned resources, advanced and automated aseptic processing systems, operational excellence and a thorough understanding of the market dynamics that effect parenteral drug markets. In 2007, Laboratorios Grifols was one of the first companies in Europe to obtain authorization for parametric release for its two EMA- and FDA-certified production plants covering more than 15,000 m² in Barcelona and Murcia, Spain. Parametric release is a guarantee that the product has attained the desired quality and is based on the information collected during the manufacturing process in compliance with the specific demands of the Good Manufacturing Practices (GMP). This recognition was received thanks to the rigorous quality system at Grifols, which guarantees the sterility of the product without the need to carry out additional sterility tests.

CDMOs with experience in meeting regulatory specifics globally, as well as those well versed in parenterals through the product's lifecycle, will be the ones most qualified to provide the strategic counsel required to attain market success. Grifols Partnership is uniquely qualified in this case and any strategy that involves attaining or sustaining market and patient success for a parenteral therapy will benefit from the association. **P**

→ ABOUT THE AUTHORS



Marga Viñes Business Development Manager, Grifols

Marga Viñes holds a degree in pharmacy and an MBA in pharmaceutical management from the University of Barcelona. She has more than 15 years' sales and marketing experience in the pharmaceutical industry and healthcare business, defining and implementing marketing strategies for international and domestic markets. In addition, she has nine years' experience in the field of strategic marketing and business development in the contract manufacturing business on an international level.

LinkedIn www.linkedin.com/in/marga-viñes-a9aa748

Email marga.vines@grifols.com



Oriol Prat Director Contract Manufacturing, Grifols

Oriol has been working in pharmaceutical marketing and sales, with a focus on the hospital business both domestic and internationally, for 30+ years. He has spent the last 15 years devoted to the strategic business growth of products and markets. In the past 10 years, he has concentrated on the development of the contract manufacturing business unit at Grifols, designing positioning and communication strategy, as well as driving the company towards necessities of the market.

LinkedIn www.linkedin.com/in/oriol-prat-8952354

Email oriol.prat@grifols.com

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