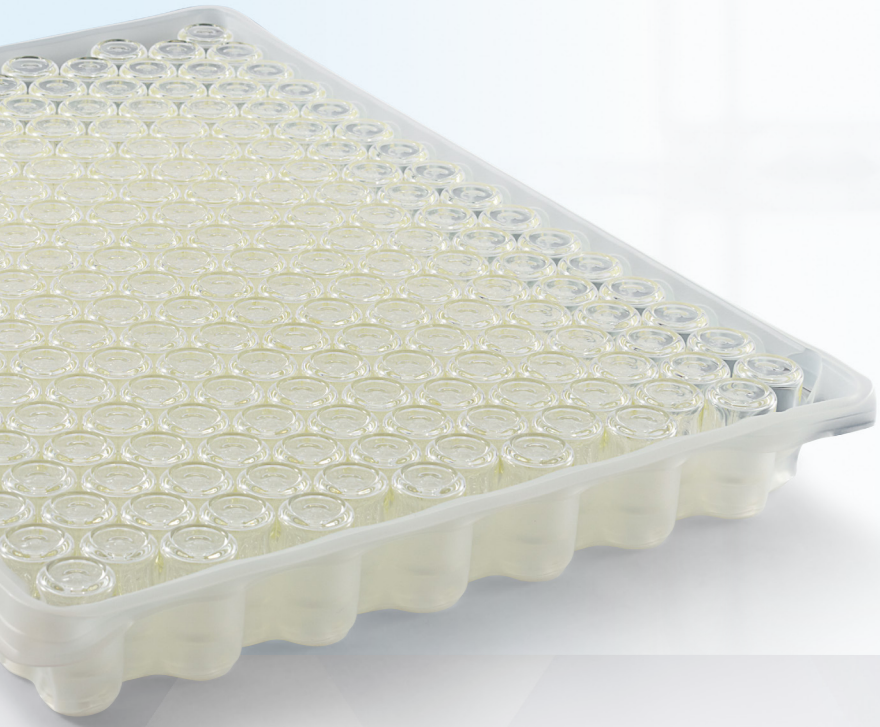

March 2023

Meeting Your Next Milestone

Containment Solutions to Help Emerging Biologic Companies Get Products to the Market Faster

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Executive Summary

Compared to large biopharmaceutical manufacturers, emerging companies have unique challenges when it comes to bringing an injectable biologic to the market. Yet their overall goals are the same as any drugmaker: accelerate overall speed to market and streamline the regulatory approval process.

This white paper will review the top challenges that emerging biologics companies face and will present packaging containment offerings and services that help mitigate risks and reduce obstacles that slow development.

Meeting Your Next Milestone

Containment Solutions to Help Emerging Biologic Companies Get Products to the Market Faster

The number of approved biologics is helping to grow the treatment options available to patients. Emerging companies are driving this growth through the development of new molecules that are at the heart of impressive leaps in medical innovation.

Emerging companies are small or newly formed organizations and have unique challenges compared to larger biologic companies. They need access to adequate funding, are heavily reliant on outsourcing, and have limited resources to support many of the activities needed to bring a drug to market. While emerging companies are smaller in size and may face different obstacles than larger and more experienced companies, these segments share two common objectives for drug development: overall speed to market and regulatory approval.

This white paper will review dynamics in bringing an injectable biologic to market and will focus on the top challenges that emerging companies face. This paper will provide solutions on how to set your small company up for long-term success using packaging containment offerings and services to help mitigate risks and speed up your time to market.

Biologic Market Trends

The number of biologic molecules in the pipeline and increasing competition among drug developers are helping to grow the biologics market.

There Is a Rise in the Prevalence of Biologic Therapies

The biologics pipeline grew 14% from 2017 to 2021, outpacing small molecule development, which only grew 5% in the same period.[1] Advances in biologic therapies, new technologies, and faster drug approvals are driving this growth. Biologic molecules comprise ~60% of FDA drug approvals per year, with a total of 48 biologic drugs approved in 2021, nearly three times higher than the number of biologic approvals in 2011.[2]

Emerging Companies Are Driving Pipeline Growth

Emerging companies are responsible for the R&D growth in these biologic programs, holding 80% of the 3,100 pipeline candidates as of 2021.[1] Investor funding, the FDA's acceleration of drug review and approvals, and incentives for the development of orphan drugs are all factors leading to favorable market conditions, making the biologics market attractive for new companies.

Competition Is Intensifying

The number of biologics companies with pipeline programs has nearly doubled in the last five years, greatly increasing competition in the market.[1] New companies are largely focused on the same key areas, with 72% of the biologics pipeline programs targeting four main therapeutic areas.[3] A growing number of market entrants, an increasingly crowded therapeutic space, and more drug approvals are further increasing competition and growing the biologics market.

CHALLENGES IN DRUG DEVELOPMENT

While these trends are creating a favorable market for the growth and expansion of biologic treatments, there are challenges with developing and bringing a biologic drug to market. The estimated development cost for a single FDA-approved drug is $2.6 billion, and the process could take an average of 10 years.[4,5] Although a significant amount of time and money are invested into R&D programs, only 10% of drugs in clinical testing ever even make it to FDA approval.[6]

In West Pharmaceutical's 2021 Packaging Thought Leader Insights Survey, more than 50% of respondents from emerging companies ranked these items as top challenges:

1. Ability to meet short timelines
2. Increasing regulatory demands
3. Limited resources and expertise

Developing strategies early on that can accelerate your timelines without increasing risks to your company and your patients later on in the journey is essential. For example, what is the downstream impact of a missed milestone? Is funding heavily tied to meeting your next milestone or will you face risk with a larger acquisition deal? What are the repercussions to the health of patients that are waiting for these treatments?

With everchanging regulations and increasing scrutiny, it's challenging to keep up with the standards and achieve compliance with regulatory requirements. Although there are regulations, guidance, and compendia in place, there is no "one-size-fits-all" approach to qualifying your packaging system. How will you navigate growing regulatory complexity and requirements to ensure compliance?

Evaluating primary packaging for your drug product is challenging, and for smaller companies with limited resources, properly qualifying a packaging system can become increasingly difficult. You may be faced with having to spend extra time and energy researching and qualifying packaging, which could take resources away from other critical areas of your drug development. Decisions around where you focus your internal resources could impact the overall success of your program.

Challenge #1: Ensuring Expedited Speed to Market

Did you know that emerging companies take an average of two to three years longer to get their drug products to market, compared to mid- to large-sized companies?[7] Speed to market will likely determine the market share you acquire. Deadline pressure in early phase development is important as you need to meet project deliverables on time and progress to the next key milestones without delays.

Delays (see Figure 1) can be costly, bringing risk to your launch and impacting the long-term profitability of your drug. Each day that a drug's launch is delayed costs an average of $1.1M in potential lost sales.[4] Delays can also impact a company's ability to recoup R&D investments, waste valuable drug-patent life, allow competitors to take market share or rise to the top market share position, and negatively impact patients needing these treatments.

Regardless of a company's size, recognizing the importance of packaging development and prioritizing its role in your drug development early on can help you identify events that could delay your timelines, so that you develop proactive strategies to overcome these risks.

For example, have you thought about how making decisions for your packaging system early on could help you mitigate risk and expedite your overall speed to market? When testing and selecting packaging options you could encounter

FIG 1

WHAT CAN DELAY YOUR SPEED TO MARKET?

- Selecting a packaging system that is incompatible with your drug
- Investigating quality failures
- Supplier delays
- Lack of expertise or resources
- Missing milestones
- Missing key project dates
- Challenges with scale-up moving from R&D to commercial production
- Regulatory filings for global markets

challenges such as delamination, insufficient containment, or unknown extractables and leachables with your component selection. Quality, regulatory and formulation challenges are easier to manage when considered early in pre-clinical or Phase 1. Doing the necessary work upfront, such as investing in proper packaging and resolving known issues will position you well for Phase III, when you need to have selected your containment system. You can then continue through your development with a packaging solution you know will work for your drug, allowing you to focus on other critical areas for launch. Using the same components enables your drug and its packaging to maintain a consistent profile through the drug development cycle and can simplify your regulatory path, as you may not need additional regulatory filing or amendments when you scale up for commercialization.

Early on, you should consider other needs you may have for scaling up your product. Scale up alone can be easily underestimated. Are the packaging components available in larger quantities? If you are outsourcing commercial manufacturing to a third party, are your packaging components compatible with their filling equipment? Selecting a system that is incompatible with your drug or extra time spent investigating quality failures with your packaging system could slow you down. Taking a longer-term view on mapping out the risks in drug development can mitigate program delays downstream.

Challenge #2: Staying Updated with Regulatory Changes

As regulatory scrutiny increases, there has been a stronger focus on quality requirements regarding how drugs are packaged and delivered. Primary packaging is not typically a smaller drug company's core area of expertise, so navigating the regulations could be a daunting task.

For example, have you thought about your extractable and leachable (E&L) strategy and the impact to your timelines? Demonstrating the compatibility of any material that comes in contact with a drug product throughout its lifecycle (manufacture, containment, and delivery) is a requirement for any regulatory submission. Agency expectations on this material evaluation, defined as extractables and leachables, continue to evolve and expand. These expectations are well beyond a check box activity that can be quickly and mindlessly completed at the end of Phase III. Newer companies are often at a disadvantage from larger companies as they do not have the ability to leverage historical E&L data or the advantage that comes with a platform approach to containment needs. Unfortunately, West sees a pattern where new and emerging pharmaceutical companies wait until the end of Phase III to start planning their E&L testing program. Waiting this late in development can lead to increased costs and delays, stemming from poor assessments that are questioned by the reviewer, or incomplete submissions that require the drug company to redo or execute additional work. In order to meet regulatory expectations, the mindset around E&L testing must change from "How quickly can we get extractable and leachables testing done?" to "Is it too soon to start my extractables and leachables assessment?"

FIG 2

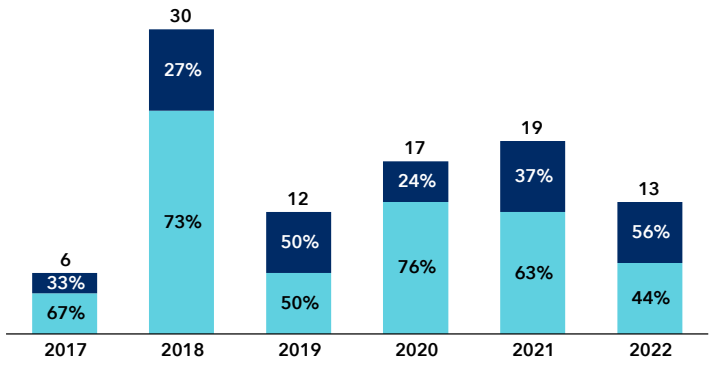
STAYING UPDATED WITH REGULATORY CHANGES

Constantly changing regulations and expectations place the burden of proof on drug companies

ICH Q8	USP <788>	USP <1207>
ICH Q9	USP <790>	USP <800>
ICH Q10	USP <1663>	USP <1663>
	USP <1664>	USP <382>

FIG 3

REASON FOR INJECTABLE PRODUCT RECALLS[1]



1. https://www.fda.gov/drugs/drug-safety-and-availability/drug-recalls (Accessed September 1, 2022) and https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/recalls-biologics (Accessed October 17, 2022)

Constantly changing regulations and expectations are placing more responsibility on drug companies to prove that both their drug constituents and primary packaging are safe and effective. Figure 2 shows some examples of the many relevant FDA guidance documents and USP requirements for injectable drug containment.

Regulatory complexity will not dissipate with time, and failure to understand or comply with the ever-changing requirements could cause a regulatory agency to deny your submission or require additional data, bringing risk to your program, such as delays to your timeline or missing a key milestone tied to an acquisition deal.

Approved drugs can fail to maintain their product quality. When reviewing the reasons for drug recalls, the FDA documented that foreign particulates, combined with the potential lack of sterility, accounted for 34% of product recalls from 2017 to 2022[8,9] (see Figure 3). This consistent theme is a major driver for regulatory agencies increasing their expectations of product quality. Contamination can have severe consequences for patients. Ultimately, you will want to reassure yourself and prove to regulators that your packaging protects both the drug product and the patient.

Challenge #3: Managing Limited Resources

With a leaner organization, it is important to make efficient use of limited resources. Many factors are important to consider when selecting a container closure system (see Figure 4), and once selected, you will also need to complete a thorough evaluation of the primary packaging to demonstrate how well it works with your drug. Regulatory agencies make decisions based on real data, so it is critical to have supportive data and documentation for your selected primary packaging.

Common mistakes that drug developers may make when qualifying a packaging system include:

1. Failure to maintain container closure integrity (CCI), which ensures the system is properly sealed throughout the life of the drug, protects the drug from contaminants, and prevents product loss.
2. Identifying and controlling particulate contamination risk is addressed too late in development.
3. Failure to properly assess and test for extractables and leachables.

Outsourcing and leveraging external expertise that can guide you in selecting the right containment system and relevant tests needed can help you avoid mistakes that could cost you extra time and resources later in the process. For example, unexpected extractables would force additional tests to discover the source of and relative importance of contaminants. Unexpected drug sensitivities could have consequences as serious as forcing you to reevaluate your primary packaging choices.

Taking a proactive approach to your packaging strategy can improve the success of your drug launch.

Areas to consider include:

- Mapping out your testing plan to service the regulatory authorities you will be applying to
- Researching proven solutionsin the market
- Future-proofing with a highest quality philosophy

Another common mistake new drug companies make when selecting components is to outsource the decision to their CMOs who do not always have the deep expertise or knowledge of all the various primary packaging options. CMOs may recommend components based on their current inventory or what they have used for past filings, but these options may not be best suited for your drug product. These recommendations could bring risk to your program, as there is no one size fits all decision for packaging system. The packaging system that you should use should be driven by the need of the molecule and what components are best suited to protect and contain the drug. Additionally, the wrong decision could lead to operational inefficiencies later on in the fill finish process such as sticking and interlocking of stoppers during filling operations leading to high reject rates. Working with a packaging supplier early on to assess the right components that will protect your drug product and enable a smooth fill finish operation. By leveraging the expertise of your primary packaging component supplier early in the process you can avoid mistakes that could cost you extra time and money later in the process.

What if you could overcome challenges that could potentially slow you down by focusing on packaging solutions early on in your development? Those solutions are covered in the next section.

FIG 4

MANAGING LIMITED RESOURCES Outsourcing and leveraging external expertise can help you navigate complex questions:

- How will you protect your biologic drug?
- What packaging configurations do you need?
- Are you selecting the highest quality?
- Will you meet your timelines?
- How will you ensure patient safety?
- Can you effectively scale up?
- How will you demonstrate container closure integrity?
- What markets do you want to enter?

SOLUTION #1:
Containment Solutions to Facilitate Your Development

The West Ready Pack™ Containment System

West's Ready Pack™ containment system (Figure 5) is an ideal solution for an emerging company in need of a proven containment system for a biologic molecule. It is designed to protect your drug, providing high quality and consistency throughout your development. This complete system includes ready-to-use stoppers, seals, and vials that meet USP, EP, YBB, and JP pharmacopeia requirements, serving you well in both clinical stages and scaling up to commercial quantities.

The Ready Pack™ containment system is the packaging solution for early development which helps you to overcome challenges discussed here, such as mitigating regulatory risks and increasing your speed to market. The Ready Pack™ containment system combines high-quality components, proven as a system to protect, store, and enable the delivery of your drug product, providing you with these benefits:

- Proven system with CCI to give you peace of mind that your components work together
- Components are supplied sterile and can be directly introduced into your or your CDMO/CMO's filling operations, eliminating extra processing steps and time
- High-quality components designed to meet regulatory expectations in the market
- Supplied directly from West, eliminating the need for you to work with multiple suppliers.
- Enables easy scale-up from clinical to commercial quantities
- Simplified regulatory path, with no additional regulatory filings or amendments
- Small quantities, avoiding waste associated with commercial volumes
- Easy ordering and quick delivery of stoppers, seals, and vials from a single supplier

FIG 5

ONE PACKAGE, ONE SOURCE, ONE DECISION
Proven vial containment that scales from R&D to Commercial

West READY PACK™
Ready-to-Use Sterile Packaging Solution

The West Ready Pack™ Containment Solution offers superior quality components to protect, store, and deliver your drug product. Multiple options are available for stoppers, seals, and vials to provide you with components best suited for your molecule.

Vials

Daikyo Crystal Zenith® polymer vials resist breakage, eliminate delamination risks, and have low particles. They are ideal for high-value drugs, cryogenic storage, and are proven to contain advanced therapy applications, such as gene therapies.

Corning® Valor® RTU Vials with Stevanato Group EZ-fill® technology resist breakage and crack generation, eliminate the risk of delamination, and reduce particulate generation. These vials provide the ultimate protection for high-value drugs and high-breakage processing, such as lyophilization applications.

SCHOTT adaptiQ® are gold standard borosilicate vials in a pre-washed and pre-sterilized ready-to-use (RTU) configuration, provided in a highly standardized secondary packaging.

Seals

Flip-Off® CCS (Clean, Certified, Sterilized) seals have specified particulate and bioburden levels that ensure compliance with European regulatory guidelines for aseptic crimping.

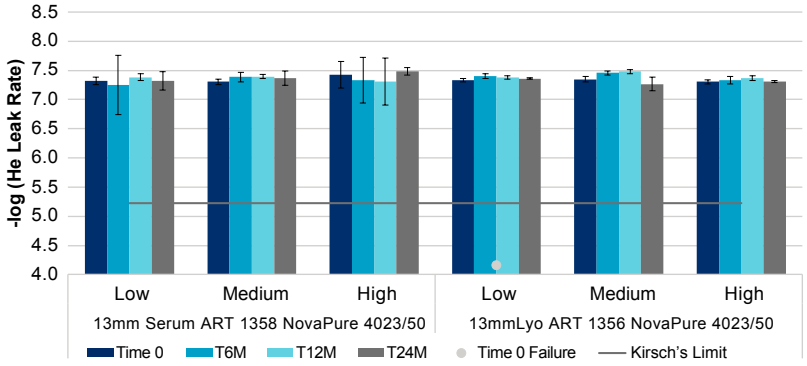
Stoppers

NovaPure® stoppers help mitigate your risk by protecting lyophilized and serum liquid drugs from visible and subvisible particles and unwanted stopper interactions.

Daikyo D Sigma (DΣ)™ stoppers combine advanced technology and expertise to provide the tightest particulate specification in the Daikyo portfolio and 100%-dimensional verification, helping to reduce variability and mitigate potential risks to patient safety.

FIG 6

AVERAGE REAL-TIME HELIUM LEAK FOR 13 mm SYSTEMS[1]



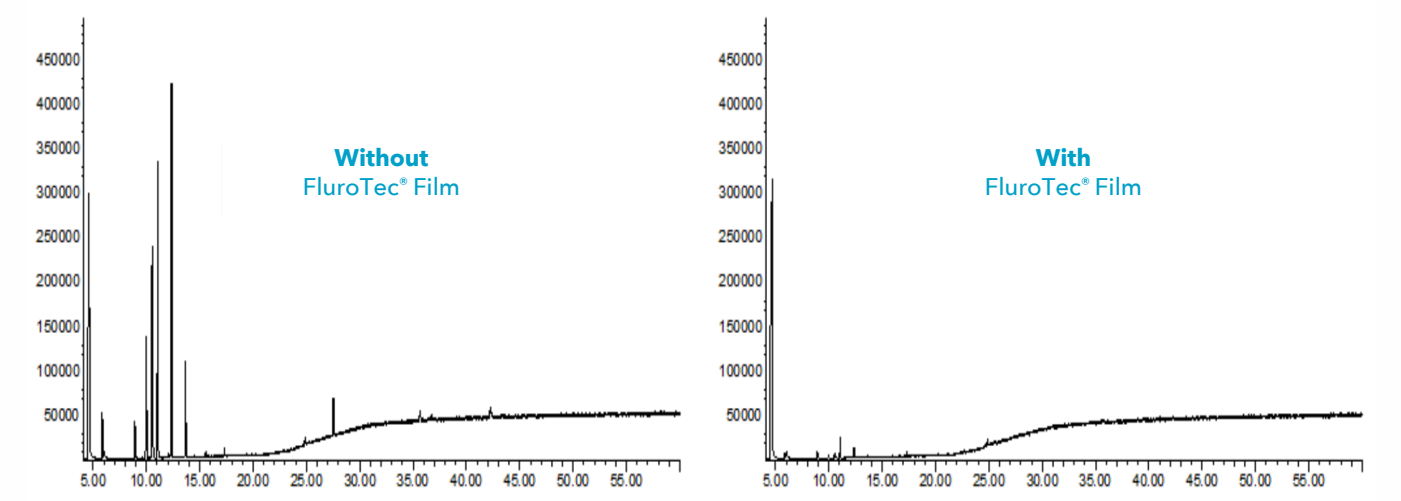
Proven Container Closure Integrity

Container closure systems should maintain the sterility and product quality of final drug products throughout their shelf life. Trying to find vial components that are proven to work as a system and can service you as well in the clinical stage as at commercial quantities, can be a barrier to success. You can eliminate that barrier by using West's Ready Pack™ containment system, which offers vial components that are designed to work together as an integrated system with proven CCI.

Results of the CCI test performed by tracer gas leak detection with helium, a deterministic method

FIG 7

HEADSPACE CHROMATOGRAPHY AFTER SIX MONTHS



recommended through guidance (see Figure 6), show four of West's Ready Pack™ containment systems evaluated over two years. All of the bars are higher than the limit indicated by the dark grey line, meaning the system does not leak gas, passing the acceptance criteria for this CCI test. These extended CCI studies demonstrate excellent performance of all evaluated West Ready Pack™ containment systems over two years at room temperature.

NovaPure® Stoppers Meet or Exceed Particulate Standards

Subvisible particulate continues to be a significant patient safety concern, and global regulatory agencies' expectations are for both the drug and the drug packaging to be essentially free of particulate. With NovaPure® stoppers, you can meet or exceed rising particulate standards and lower your risk of particulate-related rework and costs. The controlled manufacturing process sets a higher standard for visible and sub-visible particles and visually inspects every component, so your team can stay focused on advancing your complex molecule rather than stopping to investigate particulate issues.

FluroTec™ Film Reduces Drug Interactions

NovaPure® stoppers are coated with FluroTec™ film, a well-known barrier which has gained global acceptance and has been selected for use in packaging in more than 130 drug product approvals.[10] Clinical experience and migration studies have shown that FluroTec™ film successfully reduces the risk of chemicals migrating from elastomers into the drug product.[11] Headspace chromatography data show a significant difference in the way a non-laminated stopper performs compared to a stopper with FluroTec™ film (see Figure 7). Empty vials were closed with stoppers that either had or did not have a FluroTec™ film coating and then capped. Vials were then stored in upright position at 25°C/60% RH and tested after six months. The samples were analyzed using headspace gas chromatography coupled with mass spectrometry for volatile organic compounds (VOC).

The non-laminated elastomers, displayed on the left, showed approximately eight VOC peaks exceeding >0.5µg/unit. Elastomers with FluroTec™ film, shown on the right, did not show any peaks >0.5µg/unit. The effectiveness was demonstrated for the volatile compounds, and these data illustrate suppression of VOCs by FluroTec™ film, reducing risk to both the drug and patient.

Convenient and Simplified Purchasing Process for West Ready Pack™ Containment System

The Ready Pack™ containment system is a complete containment solution to support you from early-stage development to scale up. Multiple options are available for stoppers, seals, and vials to provide you with components best suited for your molecule. Components are available in small quantities, providing you with the flexibility to buy the full system or only the components that you need, reducing waste associated with commercial volumes.

SOLUTION #2:
Services to Simplify Your Journey to Market

Analytical Lab Services Support

Selecting and properly qualifying your primary container system are both critical activities for getting your drug approved. There are many considerations for vial containment system testing such as:

- Extractables
- Leachables method development and method validation
- Container Closure Integrity
- Particle analysis

Navigating the proper tests and data required for approval can be challenging (see Figure 8). Although there are regulations, guidance, and compendia in place, there is no "one-size-fits-all" approach on qualifying your packaging system. Working closely with a partner that can help guide you through these challenges and provide technical support throughout your process allows you to focus and make the best use of your available resources. West has almost 100 years of experience in primary packaging. Our Analytical Lab Services team brings knowledge and scientific expertise to guide and support you through containment requirements, allow you to focus your resource and time on your core drug development.

FIG 8

CONSIDERATIONS FOR VIAL CONTAINMENT SYSTEM TESTING

SUMMARY

Emerging companies are at the forefront of science and modern-day research. But more players entering the market means more competition, increasing the importance of speed to market. Not only are you under pressure from increasing competition, but you are under the clock to appease investors, obtain approvals, and launch your drug. You must do all these things while not compromising patient safety.

As you embark or continue on your drug development journey, West can support you with solutions to overcome potential challenges you may face:

1. Accelerate your path to market

The West Ready Pack™ containment system is a proven solution, designed to meet the needs of small companies in early stage, delivering components to your site quickly and with easy scale-up when you are ready for commercialization.

2. Minimize regulatory risk

The Ready Pack™ containment system provides quality assurance for your biologic drug and peace of mind that components work together with proven CCI. It includes West's highest quality components, including NovaPure® stoppers with FluroTec™ barrier film, designed for meeting regulatory expectations in the biologics market, such as reducing particulates and leachables.

3. Free up your limited resources

You can take advantage of the broad array of services, such as analytical testing and regulatory support, available to help you at any stage of drug development. Our global sales and technical support teams are dedicated to supporting emerging biologics customers in any region, helping you navigate technical and regulatory challenges and provide you with solutions, allowing you to focus your efforts on drug development.

West's Ready Pack™ system provides you various options of high-quality stoppers, seals and polymer or glass vials for a complete system, designed to protect your drug, providing the assurance of high quality and consistency throughout the development timeline. West's Ready Pack™ system components are supplied ready-to-use, pre-tested and proven to maintain container closure integrity. This containment system was designed to allow you to transition from early-stage drug development through to approval, providing a high-quality solution that will help mitigate your risks and get to market faster.

If you would like to learn more, please visit the West Ready Pack™ containment system page where you can access more information such as product brochures and case studies.

We invite you to Contact Us so that we can connect you with an account manager in your region or visit our online store, an easy and convenient way for you to order West Ready Pack™ containment system components.

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REFERENCES

1. Pharma Circle Pipeline Comparison. Format Injection, Biologics. Results of data analysis performed by authors.
2. Pharma Circle: Number of Novel Injectable FDA Approvals. Results of data analysis performed by authors.
3. Kent, D., Rickwood, S. & Di Biase, S. (2017). Disruption and maturity: The next phase of biologics [White paper]. QuintilesIMS.
4. DiMasi, J.A., Grabowski, H.G., & Hansen, R.W. (2016). Innovation in the pharmaceutical industry: New estimates of R&D costs. Journal of Health Economics, 47(20-33).
5. Pharmaceutical Research and Manufacturers of America (PhRMA) (May 2015). Biopharmaceutical Research & Development: The Process Behind New Medicines.
6. Biotechnology Innovation Organization (2021). Clinical development success rates and contributing factors 2011-2020.
7. IQVIA Institute (2019). Emerging biopharma's contribution to innovation.
8. U.S. Food and Drug Administration (FDA) (2022, September 30). Drug recalls. U.S. FDA Retrieved September 1, 2022, from https://www.fda.gov/drugs/drug-safety-and-availability/drug-recalls
9. U.S. Food and Drug Administration (FDA) (2022, August 5). Recalls (biologics). U.S. FDA Retrieved September 1, 2022, from https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/recalls-biologics
10. Drug approvals based on Letter of Authorization (LOA) records.
11. West Pharmaceutical Services, Inc. (2019). FluroTec™ Products Protecting Drug Product Quality and Safety. Technical Report 2019/210.

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