Pharmaceutical Packaging Primer: Focus on Primary Packaging and Drug Delivery Systems for Injectable Medicines

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Panelist: Heino Lennartz, Former Vice President and General Manager, Global Pharma at West Pharmaceutical Services
Moderator: Shane Sullivan

AGENDA:

- What are the key categories of primary packaging components and drug delivery systems in the realm of injectable medicines? What is the current size of the market? How is demand growing across each category?
- Who are the leading manufacturers of primary packaging components and drug delivery systems for injectable medicines? How do companies like West Pharmaceutical Services and Gerresheimer differentiate themselves?
- What is the business model for manufacturers of primary packaging components and drug delivery systems for injectable medicines? How do pricing, contracts, and buying criteria work in this space?
- What are the key risks and growth opportunities for manufacturers of primary packaging components and drug delivery systems for injectable medicines?

OPERATOR: Hello, and welcome to Guidepoint's *Pharmaceutical Packaging Primer: Focus on Primary Packaging and Drug Delivery Systems for Injectable Medicines* with Heino Lennartz. The statements or opinions expressed today are those of the Advisor and not Guidepoint, who disclaims all liability for the content provided. The Advisor may not disclose material nonpublic or confidential information or any information that would cause the Advisor to breach any duty or obligation. Guidepoint is not a registered investment advisor and the information provided is not intended to constitute investment advice.

I would now like to turn the call over to your moderator today, Shane Sullivan. You may begin.

Shane Sullivan: Hello, everyone. Good morning, and thanks for joining us on today's primer call concerning the pharmaceutical packaging industry. We're going to focus on injectable

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medicines. Before we get started, just a few housekeeping items for those in the audience listening in. First, if you have any questions that arise over the course of the discussion that you would like me to relay anonymously to the Advisor on your behalf, feel free to email us at Ask@Guidepoint.com, and I would be more than happy to do so. In addition, this is a primer, so we will primarily be reviewing the basics of this industry. I would encourage those on the line to stay tuned for more detailed discussions we will be hosting in the future.

With that, Heino, I'd like to thank you once again for joining us today. It should be an interesting discussion. To begin, would you mind introducing yourself and providing us with an overview of your background, please?

Heino Lennartz: Thanks very much, Shane. My name is Heino Lennartz. I worked for West for more than 12 years, so in the healthcare industry, in different roles, starting as the European CEO, overseeing all the European businesses, and being also in charge of the entire diabetes field. Then I took over when we have changed the organization toward a more customer- and market-focused organization, from a regional business into a segment business or business unit business. I took over the branded pharma, if you will, business unit and was responsible globally for the entire branded pharma plus specifically the diabetes sector. I left West in 2018, and since then, I'm a self-employed business coach and consultant. Thanks for having me.

Shane Sullivan: Thank you. Absolutely. Heino, the aim of this discussion is to review the basics of the pharmaceutical packaging industry within the realm of injectable medicines. Starting out, what are the key categories of packaging for injectable medicines? Maybe you could also explain to us the difference between primary packaging and secondary packaging.

Heino Lennartz: I think I'm distinguishing most of the time in small-volume category and larger-volume category because that drives a little bit the packaging components. I think we will talk about predominantly the small-volume ones, which is up to 100 ml, and we are having here primary, secondary, and tertiary packaging.

What I mean by that is primary is everything which is deemed to touch the product: means the container, the plungers, the stoppers, and even sometimes also the surrounding — when you talk about plastics, you potentially have also an interaction with the labeling on the plastic syringe, and we'll come to that later potentially again. Everything which touches directly the product is deemed to be primary packaging.

When we talk about small-volume categories, we're talking about vials, prefilled syringes, cartridges, or ampoules, which are then the smaller-volume categories. I would say roughly 50% of the small volumes are coming in vials, and 35%, which is strongly growing, in syringes at the moment, so that we have a good understanding. The rest is coming in cartridges, or let's say 15%, 10% potentially, in ampoules. Cartridge is a specific — we will talk about that, I think, later in that call because most of the time you need a delivery device for the cartridge in addition.

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Shane Sullivan: Perfect. While we were having our pre-call discussion, you mentioned this thing called a master file. How is that relevant to pharmaceutical packaging?

Heino Lennartz: Everything which is injectables or also in oral forms as a drug or medicine, and you want to apply that into the market, you need to pass the registration and filings. The filing is called drug master file at the FDA, and there are procedures how to pass that filing procedure. Before you haven't passed that and registered your drug, including — and here's the important thing — including the packaging, because primary packaging belongs to the product, efficacy studies, data packages, risk analysis, all of that needs to go into the filings. Then the regulatory bodies are looking at that and say, “Yes, that's fair. We can apply that to the patients because we have done risk studies and so forth,” or even not. This is then the regulatory environment you need to pass.

Shane Sullivan: Got it. Heino, moving on, is there any way to frame what percentage of overall drugs are administered via injection versus other administration routes: oral, for example? Has that been holding steady? Has it been increasing? Has it been decreasing? Just trying to get a better sense for some of the demand drivers in this space at a high level.

Heino Lennartz: I think the English term for that is “parenteral,” so everything which doesn't need to apply over your column is then the injection. If you see most of the product, when you come to vaccination, oncology products, monoclonal antibodies: everything is coming as the blockbusters of the future normally in injectable format. There are hardly really blockbusters from an oral perspective at the moment, or I haven't seen that over a couple of years in the meantime. Most of that, and specifically customized drugs, are coming in injectable form. That's why I think the increasing specifically in the biologics and biosimilar sector is clearly in injectable form.

Shane Sullivan: How large is the market for primary packaging in the realm of injectable medicines? Have suppliers, whether that's for containers, closures, delivery devices in some instances, have they been growing in line with the broader pharma space in terms of the injectable medicines piece of that?

Heino Lennartz: I think, when you look into the data which are publicly available at the moment — and we talked about that, Shane — a little bit an unknown is what is the capacity increases we've seen specifically in glass manufacturers for vials or syringes due to the COVID crisis and effect. I think the market size on a prefilled syringe base is around $20 billion as a sales market for the prefilled syringes, and they are steadily growing. I think the CAGR there is around 6%, 6.5% going forward over the next 10 years. For the vial market, we're talking about $6–$7 billion market, and clearly, that's the sale market, and that is growing up to $10 billion by 2032, which is a CAGR of a little bit more than 5%.

That really then drives the demand of the packaging components. When we're talking about packaging components, if in the likes of a syringe, we have a plunger and a needle shield or a tip cap on top, and when it comes to the vials, we have a stopper on top of it and then a kind of crimp

cap which is holding then the stopper to the neck of the glass, this is then driving the demand of the packaging components.

Shane Sullivan: What types of injectable drugs correspond to these different categories of primary packaging? What I mean by that is — you mentioned that the majority of the market is still vials, but syringes are growing. What comes in vials? What comes in prefilled syringes? What comes in these cartridge-based systems, which is still small, but growing, I think you said, when it comes to injectable medicines?

Heino Lennartz: We'll talk about cartridge in specific, I think, later on again, but let me start — what I think is the real differentiator is multidose or single dosing and the application then to the customer. That's one of the drivers.

When we look into the primary packaging, I think all injectables can come into different formats. Most of the time, the pharma company starts with a vial and have already a development for a syringe, and potentially also a delivery device on top of it because they can earn much more money with the with delivery devices and syringes than with a multidose vial. That's why, for example, the market is talking about shifting the COVID vaccination from multidosing to single dosing in order to have also more value to the customer and ease to access, I think in the pharmacies or at the doctors that they don't need to change that.

Nearly every injectable can come in different formats, but the driver is: is it a multidose, is it a single dose? Then the other driver is, is it a large molecule or a small molecule: means, for example, biologics are large molecules, and you need to have a gentle injection for the large molecules because otherwise it can cause pain to the patient. That's important. Diabetes, for example, as one of the market sector, is coming mainly in cartridge format. You have some still in prefilled syringes, but most of them are coming with cartridges and then pens.

Shane Sullivan: Digging into these different component categories here, I want to talk about the containers. I know vials, syringes, cartridges, they can come in either plastic or glass. What tradeoffs do customers consider when choosing the material for the container? Does it come down to storage requirements? Are there differences in leachability?

Heino Lennartz: I think here, important — if you really look into the market, the plastic portion is still very small. I would guess that the plastic portion is not more than 10% in most of the areas at the moment, growing due to the COVID impact because there was also some fast-track registration of plastic packaging together with some of the drugs because, simply, it was a shortage in glass.

What is really driving what you want to use, glass or plastic, are the different technical features. Here, you mentioned it already. Extractable profiles and leachable profiles are important: means everything which is the drug is contained in — means glass, plastic, or even also the elastomeric stoppers — you need to check whether something is sucked out of the drug that the efficacy of the drug is going down or is diluting the drug. For example, permeability in plastic is an issue for

some of the drugs who are very sensitive to oxygen. Then you have other things like iron when it comes to needles and the combination with needle.

Primary packaging in itself also is important from price versus injection. If the packaging component plastic is more expensive than the glass, you potentially have chosen glass. The other thing is when it comes, for example, to a syringe, some of the products are sensitive to silicone oil. You need, in a glass syringe, silicone oil in order to move the plunger. That's different in a plastic syringe. Technical things, leachables, risk profile: all of that is driving then the definition of what container technology, glass or plastic, we are using.

Shane Sullivan: Understood. Thanks for explaining that. Very helpful. I was hoping you could expand on one of the comments you made just a bit ago, which is — one development I've read about has been ongoing shortages to pharmaceutical-grade glass used in the production of vials and other containers, specifically type I borosilicate glass. What has been the impact on these container suppliers? You mentioned that some plastic components have been fast-tracked as a result. Is that right?

Heino Lennartz: Yes, that's true. I think here we are talking about really first-class glass which is the shortage, and that has different reasons. One is the COVID vaccination campaign. The market was completely empty with glass because you can't increase, in a very short environment, the lines or even the glass manufacturing within — I would say the investment time for that is a year, a year and a half. Even also for elastomeric parts, that's the same, a year, in order to have additional capacity upstream. I think that was one of the issues, that it is not easy to have additional capacity in the market.

There was a surge capacity in the market available, which all of the primary packaging component manufacturers need to have, but this was, I would guess, maximum 20%. Due to the vaccination campaign with COVID and the different formats, the market waand then they were looking for alternatives, and then they had fast-track approvals for plastic containers.

Again, here, the risk issue is a problem because they couldn't really give the authorities long-term stability testing, so the shelf life of that storage was much less than in glass. You had also a tradeoff with that, but due to the vaccination — it was directly gone to the market and directly injected — there was nothing really happening with the shelf life of products.

Shane Sullivan: You mentioned that plastic is still a small part of the market: 10%. Is that going to continue to grow? Are there still existing technical limitations to overcome?

Heino Lennartz: Yes, I think it will grow, but it will slowly grow. I think, also, in my active times, we have tried to substitute some areas with plastic. The problem in this whole industry is you can have wonderful new ideas, but nobody in the pharma industry wants to be the first and do something which potentially cause risk to the final patient. That's clear. You need to find, really, partners to work with in order to introduce new packaging.

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When it comes to plastic, there are so many different technical features you need to apply. For example, with Daikyo, West has implemented one plastic which is very, very unique in the market and has a lot of specialties like glass has, but doesn't have the same technical features. The question is: is the market ready also to go with new packaging components into the next decade? Because they need to develop that together then with their partners.

Shane Sullivan: We talked about containers just now and some material trends. What about the other components that accompany the different container categories we just talked about? You mentioned this a bit earlier, but could you maybe walk us through, just one more time, the different architectures — meaning what comes alongside vials in terms of stoppers, seals, all these other miscellaneous components; same deal with syringes, cartridges, and the like?

Heino Lennartz: I think I'll try to give you the architecture a little bit. Let's start with the vial. The vial is a glass vial or a plastic vial, and that needs to be closed either — there comes a differentiation with a serum stopper or a lyo stopper. A lyo stopper means you have a liquid drug in the vial that goes into a lyo chamber, a freeze-dry chamber, so the drug will be reconstituted from liquid to powder. During that process, there is a different stopper necessary than when it stays in liquid form. Then you need to close the stopper on top of the vial. In order to hold it steady in the neck, the stopper gets a so-called crimp cap on top of it. This is an aluminum cap which is crimped around the neck of the glass vial. That's the vial.

When it comes to a prefilled syringe, you have a plunger at the end of the of the syringe which is moving the liquid toward the top, and the top can be in two different formats. Either you have a so-called staked needle in it, means there is a glued needle directly into the glass, and this is covered then with a so-called needle shield. If you have not a needle on top, you have a luer-lock syringe, which is a kind of screw head, and the screw head needs to be covered then with what the industry calls a tip cap. That's the difference on a prefilled syringe.

When it comes to a cartridge, a cartridge needs also, like the syringe, a plunger, but as the top is the same format a little bit like a vial has, you need a kind of lined seal on top of it, which is a crimp cap with an elastomeric layer in it. Then this is crimped again around the neck of the cartridge. There, the needle comes in when it goes into an injection pen. Is that clear?

Shane Sullivan: Yes, absolutely. Thanks for all the detail, Heino. One concept I'm struggling with is these high-value components, so to speak: meaning, why would a customer choose a high-value stopper, a NovaPure or a FluroTec from West, over a standard component? As an add-on to that, West talks about biologic drugs, for example, being packaged disproportionately with these high-value components. Why is that? Kind of a two-parter.

Heino Lennartz: Again, here, when we look into the industry, elastomeric in itself is a dirty environment. You have iron in there; you have different chemical substances which potentially have an influence on your efficacy of the drug or even shelf life of the drug. You try to protect your drug by using the right primary packaging: means West has, for example, like also Datwyler or Aptar, a kind of barrier coating on top of the drug-faced portion of the plunger or the stopper. This

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is then a quality feature, which is a different technical foil which is coated to the elastomeric part which is a barrier coating between the drug and the dirty-stuff stopper. If you have a normal standard, this barrier coating doesn't exist, so technical differences.

Then you have — the other difference is treatment differences. It depends a little bit of the total supply chain process of the customer. Big pharma tend to do, for example, their cleanliness processes, which is — in the packaging component, the washing processes are done at the big pharma customers. Smaller customers tend to outsource that. West can do that, or Datwyler can do the washing processes for the customer: means higher value which goes to the customer. This is process-related cost.

It comes, to the end, to how it comes into the filling line of the customer. How many steps have you done yourself? How many steps have been done from your suppliers? That's driving then, also, value into the product pricing. It's either technical value because you have better understanding or supply chain value.

The third one is regulatory data: means how much data you can give about extractable/leachable profiles. Do you have an own drug master file for specific technical features? That is also bringing value to the customer because it eases their entire registration process because they can show efficacy and directly to the regulatory bodies about the packaging what they have chosen and what are the consequences with that. These three levels make a distinction between standard and high value.

Shane Sullivan: Well said. Why do biologic drugs tend to get packaged with high-value components, whether from a technical standpoint or a process standpoint or whatever? Are they less stable than their small-molecule counterparts?

Heino Lennartz: I think, when it comes to — I'll give you one example which one of my customer has told me. If you take a cancer syringe, an oncology product, the syringe, to the market, the market price is more than $1,000. Whether you pay $1 or $1.50 or $3 for the packaging, that doesn't really count from your profitability. When it comes to a diabetes product, where a cartridge of a diabetes product costs less than a can of Coca-Cola, then the differences makes a difference, so the price makes a real difference. Then you really need to think about, what kind of high value am I taking into it, and how is the cost per injection — and that's the term; the cost per injection — measured on the primary packaging component? Does that answer your question?

Shane Sullivan: Yes, definitely. Very interesting. Maybe we'll swing back to that a bit later. We talked about containers. We talked about components like stoppers, seals, plungers. Then there's a third piece to this market, Heino, which is: some suppliers in this space, like West Pharma, Gerresheimer, also offer high-value delivery systems, like pens, auto-injectors. What is driving the shift toward those types of delivery devices? You mentioned insulin, for example, being primarily administered through pens. What other types of injectable drugs come to mind for those?

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Heino Lennartz: I think, when it comes to biologics, all of the companies have biologic because from a total development perspective, most of the injectable drugs come to market in due course in the future are nearly, I would say, 60%, 70%, potentially 80% biologics: means you need to have a route of how you administer that to the patients. Also, we have a trend of home care. Both of that drives administration needs.

The interaction between a cartridge or a syringe — how you administer that in large molecules, because we are talking biosimilars or we are talking biologics, and I started talking about that already a little bit — is, then, the route of introduction into your body subcutaneously or intramuscular? If it is a large molecule, it needs to be administered very slowly and gently. To hold a syringe 10 minutes, potentially, steady in order to inject it slowly into yourself is a hard work, I can tell you, so you need delivery devices in order to get it done. Some of the delivery time per injection is more than 10 minutes. That's why you potentially need pumps, like West developed one pump, or you need injectors like — other companies have developed specific injectors for the biologic area when it comes to gentle administration into the body.

That is then really driving the upscale, if you will, and also the upstream value addition of the companies specifically looking into the biologics and biosimilar space.

Shane Sullivan: Let's switch gears once again, Heino, and talk about the competitive landscape a bit. Who are the leading suppliers across these different segments of the market: your containers, your components, and these delivery devices? Are you able to opine on the competitive dynamics, strengths and weaknesses, within each of them?

Heino Lennartz: Yes, at least I can try, Shane, and I think it's really opinion. Let’s look first to the primary packaging components, means the elastomeric and plastic suppliers: West, Datwyler, Aptar, and I name also Lonstroff and Jiangsu Hualan, a Chinese manufacturer. I think West is by far the market leader in that space, 50-plus%. I think West itself, they are claiming also 50-plus%, potentially. In the Americas market, they are much bigger, potentially 80%; worldwide, I would guess 50-plus%.

Datwyler, around 20%. Datwyler is a combination out of different branches they are working in. One leg is the pharmaceutical field, and this is an acquisition of a former company out of Belgium called Helvoet they have acquired. Aptar, I think, is number three with roughly 10%, potentially growing a little bit in the generics market because they have a lot of good generics offerings. Aptar is worldwide knowledge. They are a huge manufacturer in devices, and they have acquired a French family company called Stelmi which is very small or was very small. They are trying to get here the combination out of delivery devices and components. Jiangsu Hualan, 5%, I would say, and Lonstroff also around about 5%.

There is also a new company I've heard about — it’s called Hebei, also out of China — coming into the market. They will grow in the market as they take part of the generics piece because their price really makes a difference, but I think we come to that the drug master file is a protection shield in that market, and it's hard for new entrants to gain market share.

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When it comes to glass, I would say we have Becton Dickinson, Gerresheimer, Schott, Nipro, SGD, Shandong, and the Stevanato Group with Nuova Ompi. They have all different features and different approaches. When it comes, for example, to Becton Dickinson, one of the biggest supplier in the field of syringes and also vials into the market, they have a different business model than the other glass manufacturers. Becton Dickinson is directly working with the big pharmas, and if you are the packaging component supplier, you are a tier-two supplier. Everything goes via Becton Dickinson as a service model for the customer toward the final customer, so you are sitting not directly at the table, we called it.

With the other ones, like Schott, which has — Schott is the one with the best glass, I think, especially the glass features they have in the market. Gerresheimer has, I think, some problems in the past. They are looking for management stability. Some of the markets were resistant in order to work long term with Gerresheimer together. I think that has changed in the meantime, and they are very strong in getting now also the combination products with devices upstream.

The Stevanato Group and especially Nuova Ompi, they have also quite good glass, but they offer a different service model on top especially, and they are focused on smaller customers in the market, so startup customers, laboratories, because they have a full-service model they are developing. They can give you services on fill and finish; they can give you engineering services; they can give you packaging components and container combinations because they are working in partnerships with component manufacturers together — for instance, West. I think everybody tries to have a good market approach with their different attitudes, and Stevanato Group is very, very strong in working with smaller customers together.

Shane Sullivan: A couple of things to follow up on. I want to focus on West for a bit. Do you expect West to be able to maintain their commanding market share on the components side of things? How exactly does that master file piece of things serve as a shield for companies like West?

Heino Lennartz: I think once you have filed the packaging component and you need to reopen the filing, you need to do all the testings again. Even that there are some of them accelerated, it costs you, and that's the number I heard from our customers, between $5–$8 million, depending on how big is the change. Everybody wants to avoid even a material change because that can trigger a new filing. $5–$8 million — that's to earn with a change in the packaging component — you need to sell a lot of pieces in order to do that. Nobody is really eager to look into the different alternatives you potentially have in the market.

Once you're in, most of the time, you are in until the drug goes out of the market. A lot of suppliers have still products in place where we know that even in the market in the meantime there are much better products available, but nobody wants to reopen the drug master file, or the registration profile under European terms, because that's costing a lot of money and a lot of energy without really have additional sales. You need to have a very deemed good business case in order to persuade a customer to reopen the file.

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In essence, it's important to be there at the first second. When a product goes from Phase 1 into Phase 2, you need to know that. If they go into Phase 3, you're better in already with them; otherwise, you potentially lose that potential new drug in the market. You are investing also sometimes into areas, like also the big pharmas, where Phase 3 doesn't really survive. That's the investment you need to do in that market, and you need to work very closely with your customers. That is the protection shield I meant.

Shane Sullivan: One thing that stuck out for me concerning West in particular was its partnership with Corning for a glass. Management has talked about the industry moving toward integrated systems versus supplying individual components. Any thoughts on that partnership, why that shift may be occurring?

Heino Lennartz: I think it's important to have prime glass, and Corning has, with their latest development, the superior glass over Schott and over Nuova Ompi. That's what the market is saying. I believe that still Schott is very good in there, and West is also working with Schott. West is working with every glass manufacturer.

Here, I think when it comes to the same token I was talking about earlier, you need to concentrate on what is the best value in order to bring together different features to serve the customers potentially in a one-stop shop. The more you can offer the customer doesn't need to do himself, the more value you get out of the entire supply chain. That's the background here.

Shane Sullivan: You mentioned companies in this space differentiating on a technical basis, of course, but also on a service basis. Is big pharma in increasingly outsourcing parts of that value chain when it comes to prewashed products, sterilization-type services, things of that nature?

Heino Lennartz: I think, when you look to the pharmaceutical environment, I can give you one specific example. When pharma customers need to decide how they utilize their facilities, their footprints, they're looking in the meantime not to start directly to build a new footprint when there comes new market demand; they try in the meantime also to look around who can do things better. They have to learn a little bit how to evaluate that, really — not only looking into their variable costs, really taking care about their fixed costs.

A lot of pharma companies have started to give more of their entire value and supply chain processes, even if it is their own production process. When I talk about that, I can mention one is the crimping process. A lot of customers have done crimping themselves; in the meantime, they have shifted that back to the suppliers. This is a different process, or washing processes: a lot of customers have stopped their own washing. That's why the high-value products — for example, you look at Datwyler and also at West, they are selling much more components not longer in bulk production, so means just the prewash with the city water and that's it: even with WFI treatment, so very clean water into the production facilities, because the customer doesn't want to invest into WFI equipment. They want to invest into development equipment in order to produce their own active ingredients.

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Shane Sullivan: On the topic of pricing and contracts, one trend noted by West, Stevanato, Gerresheimer during Q3 earnings was inflationary pressures in the form of added raw material costs, supply chain costs, freight, energy costs. What is the ability of suppliers in this industry to take price over time? What has price inflation looked like historically? Have they been able to take more price than normal with the advent of COVID and all these other pressures that I mentioned?

Heino Lennartz: I think this pricing or this increase is everywhere, so it's not specifically to the pharma branch or to the pharma market. Normally, the entire market, from a packaging component perspective, talk about price per 1,000 items. That's the surrounding. The price per 1,000 items, in some of the contracts — and that's more and more the contracts over the last decades — they include a kind of index-based pricing for raw materials. For example, in the elastomeric piece, the raw material price and the price change mechanism was linked to an elastomeric index. That is also for the glass industry; they call it to a glass index. This gives you the chance to go up with the prices based on how the index is developing.

In addition to that, the normal not-linked pricing, when you have a longer-term pricing, you go back toward the customers and look for inflationary increases year over year. West has done that, for example, several times, depending on what happened into the market. For example, when we had the oil crisis, that was driving inflationary increases in the elastomeric section. That was a price increase which we went back to the customers, like also all the other manufacturers have done.

There are some mechanisms — like I explained, index based — which gives you directly the right to increase the prices, and the other one is negotiation with the customer.

Shane Sullivan: Heino, I want to talk a little bit more about COVID-19 from a couple of different angles, but to start: the mass production of COVID-19 vaccines, which from my understanding were disproportionately shipped with high-value components, has been a windfall for suppliers like West Pharmaceutical Services. West is expecting — I think it was a 50% year-over-year decline in such business next year. What is the market's ability to continue growing as demand for vaccines diminishes?

Heino Lennartz: I think, first of all, we need to talk about how that extra abnormal margin increase took place. That's not only for West; that's also for all the other component manufacturers. The market normally works with a surge capacity. Due to WHO activities, you need to have additional capacity available; due to drug shortages, you need to have additional capacity available; risk profile. The big pharmas have normally 40%, sometimes 50%, spare capacity in their manufacturing environments. The component manufacturers have less surge capacity: I would guess around about 20%, plus an additional capability to increase shift patterns and even grow it there a little bit.

West, Datwyler, and all the other have completely gone to a 24/7 operation. With that, they have increased their capability and capacities and boosted their margin levels because they didn't need to expand in fixed-cost areas, so in machinery they have done, plus the better utilization rate. They

were clearly close to, whatever, 95% because you need to do some maintenance part. With that, everyone reached that. They only could expand with the next level of investment.

In this industry, you have a fixed-cost investment up front, and then the sales come in later, but the fixed cost is every time — I call it, as a finance guy, a staged fixed-cost level. You need to invest $1 million even that you can only get an additional $100,000 revenue in the first year because you have a scale-up over the time from the different drugs you are serving then. That is then giving directly your margin a kick, and you are going down.

All the manufacturers are now in the upper scale of variable margin levels. That's my belief. They are going down when the demand is going down because then the fixed costs need to be distributed through the existing business. That's, I would say, a little bit of dilution effect we see here. Take that into consideration.

In addition to that, we need to change from — and because that's the market perspective, to go into a high-value product, as we talked about, and this needs also additional investments. We will see in the future that the fixed-cost level will increase in the environment of manufacturing, so future investments, because you can't use, in most of the cases, the old equipment to manufacture high-value products when it comes to technical features. We talked about the specific foil coating; that needs a different generation of injection presses or compression molding sets, or additional washing procedures behind that because bulk is only washed in a washing machine, but when it comes to sterilized ready-to-use products, you even need to have sterilization on top of it. That's a different ballgame in your supply chain, and that needs investment.

Shane Sullivan: One question I have is: it seems to me in terms of COVID demand — the suppliers have primarily been flexing their variable-cost efficiency gains versus fixed-cost investments, as you said. As COVID-19 vaccine demand goes down, there isn't a risk for capacity oversupply? Is that accurate?

Heino Lennartz: Yes, that's true. I don't think that if COVID goes down — and we talk about, or the market talks about, a 30%–40% reduction compared to prior year in demand. I think some of them can be absorbed by the shift also from multidose to single dose, because let's say in a vial, you have 10 shots in the meantime to the patient from a vaccination, and then in comparison, you need 10 syringes. You sell 10 times a plunger for a syringe compared to one time a plunger to a vial. That gives another kind of magnitude. You can look into it. There will be a compensation of the revenue downturn because of the switch from multidose to single dose.

Shane Sullivan: A few other trends I wanted to touch on: one thing we've been monitoring within the therapeutics space has been slowdowns in equity financing by early-stage biotech companies. Does this pose a risk for the suppliers in this space? I'm not sure how much business comes from them in aggregate.

Heino Lennartz: Like I said already earlier on, I don't think so, that it has a huge impact, because most of the time, the early-stage companies do not have huge filling runs at the moment because they're on a lab scale, and that doesn't really — or have a minor impact at the moment if they are

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not coming to fruition. I think they are getting short of equity when they are not really have good efficacy in order to reach Phase 3 or survive Phase 3. That is not really the big demand then for the packaging component suppliers.

Shane Sullivan: Likewise, another trend we've been keeping tabs on is the emergence of biosimilars. How are you viewing that impact on suppliers in this space and, really, if such compounds are any more or less likely to gravitate toward higher-value components than their innovator, so to speak, predecessors?

Heino Lennartz: I think it's a matter of filing also here. It's the same like we have also in the generics field to a certain extent. If you want to have a fast track to the market, then you potentially go with the same packaging the innovator has taken because then the filing is already existing and you can use it, so the regulatory bodies will not question too much. If you want to change that, you can do that, but that will slow down your implementation process.

When it comes to biosimilars potentially in a different format or different efficacy, then potentially, you go for the lowest risk, and you use directly the highest value you can get — like I explained, because you get all the data behind that, the risk profile is lower, and you also have a fast regulatory body approval because you want to earn very quickly money. Everything which reduces the time of registration and that the product is approved to go into the market will help you, and biosimilars are potentially also in a range of quite expensive even, so they can afford high-value packaging.

Shane Sullivan: To get a balanced view, what are the risks and challenges that one should consider when evaluating the potential success of suppliers in this space, whether that's West, Gerresheimer, Aptar, or whoever else comes to mind?

Heino Lennartz: I think you need to have in focus what is changing in the market. We talked about home care trends, for example. We talked about large molecules. I think you really need to understand what are the market drivers. In order to be there if a new injectable drug is coming into Phase 3 and potentially going into market, you need to have the service level in order to provide the customer with the right and necessary information and packaging. I think the trend to one service provider or a one-stop shop — we talked about Gerresheimer's doing that to a certain extent; Nuova Ompi is doing that to a certain extent; West is trying that to a certain extent — that is the trend.

In combination then, I think, what are the entire situation about filling? Because you need to understand if you have smaller batch technologies — let me take one example. An insulin is in an incubator filled for, I don't know, millions of cartridges in one run, whereas a biologic product has a batch size normally of 100,000 or potentially 150,000. The changeover in your filling equipment is a different ballgame, and if your filling equipment is down because you need to clean it to sterilize it, that is then lost production time. You need to help also the customer there in order to have enough production time. That's something, I think, in addition with the entire filling process.

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There, when you look into that, there are companies going in, like Gerresheimer. I think they are going in with EZ-fill components in the vial field. When you look into Nuova Ompi, they are going in with EZ-fill suites for syringes. Everybody tries to find a market space in order to offer something specific in that terms to the customer.

Shane Sullivan: Great. That's helpful. Heino, that's actually it from me in terms of questions. We haven't received anything from the audience either. Anything you add before we close it out that we may have missed?

Heino Lennartz: No, I think — first of all, thanks for having me. Hopefully, I could give you an insight into the primary packaging market. The only thing I want to touch on is some trends you might have in your focus, which is the digitalization also in that market — we haven't talked about that — because that's also important in the administration field, that people and the markets know that the patient have taken their injection, things like that. We have seen also in the diabetes sector that new glucose monitor system have changed tremendously the environment, so all the old pricking is in one time potentially over. Here also, digitalization in the primary packaging is a key we need to look at. Thanks for having me.

Shane Sullivan: Absolutely, and likewise, thanks for joining. Well, I think now would be a good time to wrap things up. Thanks so much again, Heino. I think it's been a really helpful discussion. For those in the audience listening in, if you are interested in scheduling a follow-up call, please get in touch with your Guidepoint representative; otherwise, I hope everyone has a good rest of their week and a happy holiday. Heino, thanks so much again.

Heino Lennartz: Thank you, and happy holidays and a good new year, healthy new year.

Shane Sullivan: You too.

Heino Lennartz: Bye-bye.

OPERATOR: This concludes today's conference call; you may now disconnect.