Primary Pharmaceutical Packaging & Pre-sterilised Syringe Systems – Supplier Landscape & GLP-1 Opportunity Deep Dive

13 May 2024

Key Insights

- 100% syringe market RTU. Low-/mid-single-digits for RTU cartridges and vials. Expects cartridges to shift to 100% RTU over c10 years, with an inflection in c5 following key patent expiries and replacement of legacy filling lines. Expects GLP-1 therapies to switch from autoinjectors (syringes) towards variable-dose pens (cartridges). RTU vial adoption will be slower given structural market shift away from vials
- Currently, there is a “huge shortage” of syringes and cartridges, which is expected to worsen. Customers are trying to secure any and all supply, irrespective of RTU or bulk. Such shortages could drive customers to switch from syringe/cartridge formats to vials given low barriers to switching. Such a shift to vials will be a demand driver for safety syringes, eg, sold by Nemera
- Syringe and cartridge shortages give suppliers pricing power for now. However, RTU suppliers are undifferentiated and market is fundamentally commoditised with suppliers chosen on price and supply
- More than one year’s worth of excess vial inventory in the market, mainly bulk. Hard to predict exactly when the destocking cycle will end.
- Polymer format can save low-single-digit of API volume/dose in theory, but needs validation before adoption. Will be key to offsetting commoditisation pressures in glass. No significant demand for dual-chamber cartridges

Specialist Peter Wengström (PW), Senior QA Professional at Novo Nordisk AS

Moderator Sebastian Skeet (SS), Third Bridge Sector Analyst

Agenda

- Value proposition and penetration of pre-sterilised RTU (ready-to-use) solutions across primary packaging formats, including pre-filled syringes, vials and cartridges
- Review of RTU platforms and key differentiators across suppliers, including Schott Pharma (ETR: 1SXP), Stevanato (NYSE: STVN) and Beckton Dickinson (NYSE: BDX)
- Demand outlook for polymer vs glass primary packaging across end markets
- GLP-1 opportunity deep dive for primary packaging suppliers

Contents

Q: I'd like to begin by discussing the value proposition of RTU [ready-to-use] primary packaging across the different formats. Based on previous Forum Interviews, it seems almost 100% of the syringe market uses RTF [ready-to-fill] or RTU solutions and only a low-single-digit proportion of vials or cartridges use RTF or RTU. Indeed, Stevanato Group says it's less than 5% for vials, but this is growing. Finally, ampoules are unlikely to represent a market in which there would be high demand for RTF solutions. Is that in line with your thinking? 6

Q: Over what timeframes do you expect us to reach 100% penetration of RTU in cartridges? From what baseline would that be today? 7

Q: Just so we have a point of reference, I mentioned that Stevanato assumes less than or equal to 5% penetration for the RTU format in the vial market. What would you estimate to be the penetration of RTU formats in the cartridge market? 7

Q: We have seen the roll-out of certain regulations such as Annex 1 in Europe, which applies the sterile manufacturing of therapies. While a European regulation, I understand this applies to US sites that are supplying Europe. Has the implementation of Annex 1 led to a step change in the number of manufacturing fill-finish lines that meet the sterile requirements for RTU formats? 8

Q: The key messaging from suppliers is that an RTU format allows for a faster time to market, lower TCO [total cost of ownership], higher flexibility and so on. Do you think the strength of the value proposition for an RTU platform holds true irrespective of the format, ie, syringe vs cartridge vs vial? 8

Q: Taking a step back and thinking about the value proposition for RTU formats across the different primary packaging categories, we spoke about this prior to the Interview, but cartridges and syringes are considered, at least by the regulators, as pseudo-medical devices, whereas vial is far more of a primary packaging type of format. 9

Q: Could you share a ballpark figure or an estimate for the price difference between an RTU cartridge and a bulk cartridge, and an RTU vial vs a bulk vial? 10

Q: Let's dig into the supply-demand balance for different formats, starting with syringes and cartridges. You mentioned that, in today's world, the number one KPC is security of supply and available volumes. Could you elaborate on the supply-demand balance for syringes and cartridges today, the lead times and how difficult it is to secure such volumes from the existing suppliers? 10

Q: Given the supply shortage on syringes and cartridges, I understand you're not involved in pricing discussions, but based on what you've heard from colleagues or at industry conferences, are we seeing the suppliers charge a premium for guaranteed volumes, whether RTU syringe or cartridge formats, or indeed the bulk formats? 11

Q: From a QA perspective, are we seeing any decrease in the quality of the primary packaging in exchange for increased volumes? 12

Q: I understand you're not in the procurement department, but perhaps you've been exposed to such conversations – do you have a sense for how different suppliers are prioritising allocating volumes across their own different customers? How do Schott, Stevanato, Ompi, Gerresheimer and so on prioritise their different customer buckets and determine where the majority of volumes go or who gets priority access to supply? 12

Q: Speaking about the cartridge and syringe shortages, do you have a sense for whether the current supply chain bottleneck is likely to resolve itself over the coming months, quarters or years, or do you expect the situation to exacerbate? Do you see syringe or cartridge customers having to switch to vials? 12

Q: You expect the supply situation for syringe and cartridges, whether bulk or RTU, to worsen over the near-to-medium term, to the point that syringe or cartridge customers may look to increasingly use the vial format? 13

Q: That's a nice segue into understanding the current supply-demand balance for vials, because there seems to be a fairly significant destocking phenomenon for vials, which is to be expected due to the pull forwards in demand due to the pandemic-related vaccines and the subsequent decline in vaccine production over the past few quarters. You alluded to sitting on significant bulk vial inventories. How do you see that inventory destocking for both bulk and RTU vials evolving over time, especially given what we discussed vis-a-vis customers potentially switching from cartridge and syringes to vials? 13

Q: If we look at the recent results from Stevanato, it seems the company underestimated the magnitude of in-market inventories for vials, especially if you look at what management said in its full-year 2023 and Q1 2024 results. Indeed, in the Q1 2024 results, Stevanato disclosed a 43% decline YoY in vials, and that's already following a significant decline in 2023 vs 2022. Why do you think that is? Is there inherently limited visibility in this market for suppliers such as Stevanato or did something fundamentally change from a demand perspective in Q1 for vials that led to an unexpected worsening of demand? 14

Q: When you look at the broader pharma pipeline, the number of therapies that are being developed with an autoinjector – thus requiring a syringe – or variable dose pen – and thus requiring a cartridge – is increasing relative to the number of therapies that require a vial. However, for a therapy that's currently approved and on market in an autoinjector or variable dose pen format, requiring a syringe and a cartridge, respectively, how easy is it to switch over to a vial format? From a QA, QC and regulatory perspective, or even a clinical perspective, what are the hurdles in place there? 14

Q: Let's talk about the different suppliers. Stevanato has the EZ-fill platform. However, you have Schott, Becton Dickinson, West Pharmaceutical Services and other players, all of which offer these RTU syringes, vials and cartridges. How are you thinking about the different platforms in the market and whether there are any salient differences across them? 15

Q: Based on the corporate material and marketing brochures that are out there, Stevanato claims to be the number one player in RTU vials. Who would you say is the leader in terms of RTU syringe or RTU cartridge platforms? 16

Q: We know Stevanato has a fairly large engineering business insofar as it actually ships and installs fill-finish lines. Do you think that vertical integration, which is seemingly fairly unique when you look at the competitive landscape, serves as any differentiator or driver for customer spend?	**16**
Q: I'm not too familiar with West Pharma, but if you look at the company's range of products, it seems to offer a robust portfolio of plungers and stoppers. Whereas, if you look at Stevanato's products, they're far more indexed to the glass primary packaging component itself. In a normalised supply environment, is West Pharma offering a complete product portfolio including plungers or stoppers is more of less of a differentiator? As a customer, do you select the best vendor for the glass primary packaging, the best vendor being selected for the plungers and stoppers and so on? Ie, is this one-stop-shop component as valuable as it may seem on paper?	**17**
Q: Interestingly, Stevanato sterilises its syringes in-house, whereas Schott outsources to a third-party CDMO. If I had to guess, I'd assume someone such as Steris, for example…	**18**
Q: Going back to the lack of differentiation across players, I'd like to circle back to an earlier comment you made regarding the use case of polymer vs glass. Could you walk me through the value proposition of glass vs polymer, whether COC [cyclic olefin copolymer]- or COP [cyclic olefin polymer]-based primary packaging, and which supplier you think is the leader in the polymer syringe or cartridge market?	**18**
Q: I'm not sure I understand how much traction polymer is actually getting, and over what timelines we could eventually see the switch from glass to polymer. I understand that polymer has some advantages, but as you say, there have been many projects that have fallen by the wayside. Do you see a concerted shift away from glass and towards polymer at the market level anytime soon?	**19**
Q: Do you think the shift to polymer is the solution to offsetting the commoditisation pressures we're seeing in glass primary packaging?	**20**
Q: Specialists in previous Forum Interviews have argued that Schott is the market leader for polymer syringes. Do you know much about what this company can bring to the table from a polymer standpoint?	**20**
Q: If we think about the GLP-1 [glucagon-like peptide-1] opportunity for primary packaging suppliers, at the market level, do you get the sense that the obesity market in the US will move away from autoinjectors and thus syringe platforms and increasingly towards variable dose pens and thus cartridges, given the titration needs for these GLP-1s? I believe the European market does use cartridges and pens already.	**20**
Q: We know certain pipeline GLP-1 therapies use dual chamber syringes. However, is this simply a stop-gap while co-formulation is refined. I'm curious to understand whether the market as a whole – from a patient convenience, regulatory and QA and QC perspective – wants to move away from dual-chamber- to single-chamber-device platforms, or whether you think the market is happy to accept the dual chamber technology for the foreseeable future. What are your thoughts there?	**21**

Q: Is there anything we haven't discussed today or that you would like to underline around primary pharmaceutical packaging? 21

Primary Pharmaceutical Packaging & Pre-sterilised Syringe Systems – Supplier Landscape & GLP-1 Opportunity Deep Dive

Transcription begins at 00:00:10 of the recorded material

SS: Welcome to Third Bridge Forum's Interview entitled Primary Pharmaceutical Packaging & Pre-sterilised Syringe Systems – Supplier Landscape & GLP-1 Opportunity Deep Dive. My name is Seb Skeet, and I'm delighted to have with us today Mr Peter Wengström, Senior Quality Assurance Professional at Novo Nordisk.

Peter, before we start today's Interview, please state I agree or I disagree to the following statement: You understand the definition of material non-public information and agree not to disclose any such information, or any other information which is confidential, during this Interview.

PW: I agree.

SS: Could you start with a brief introduction of your background relevant to today's Interview?

PW: I have been involved within primary packaging of pharmaceuticals since 2011-12, where I have worked on combination products for the pharmaceutical industry, mostly targeting autoinjectors and other types of handheld devices used by non-HCP users. My perspective has mostly been from a risk management and quality perspective, ensuring to reduce risk to the end user and ensure product quality.

[00:01:38]

Q: I'd like to begin by discussing the value proposition of RTU [ready-to-use] primary packaging across the different formats. Based on previous Forum Interviews, it seems almost 100% of the syringe market uses RTF [ready-to-fill] or RTU solutions and only a low-single-digit proportion of vials or cartridges use RTF or RTU. Indeed, Stevanato Group says it's less than 5% for vials, but this is growing. Finally, ampoules are unlikely to represent a market in which there would be high demand for RTF solutions. Is that in line with your thinking?

PW: It's very much in line with my experience. My experience started with the pre-filled syringes, primarily with staked needles, needle shields and stoppers. Within those projects, the request was exclusively ready-to-use solutions. Now, I have started working mostly on cartridges, which I am not so familiar with yet, but I presume that the same requirements will come into play there as have previously been for pre-filled syringes.

SS: To that point, are you suggesting that over time, you expect almost 100% of cartridges to come in an RTU format?

PW: Yes, because the volumes are growing and the need for simplicity, not only ready-to-use, but also packaged in tubs or trays that are compatible with the filling lines to make everything as streamlined as

possible.

[00:03:53]

Q: Over what timeframes do you expect us to reach 100% penetration of RTU in cartridges? From what baseline would that be today?

PW: It's a slow beast. I would say that no big changes occur over less than five years, but in a 10-year period, with the growth prognosis that is for a lot of the market, I think that we will see the... and adaptation of the same mindset as we have had for previous huge sellers like the Humira pen as the manufacturers of cartridge devices, which have previously been a lot in the insulin line of business, as they will start using other types of bolus injections.

There you have market players who are accustomed to using cartridges. Now, they will expand their scope to a lot of products that don't have the typical titration, but have bolus injections instead.

SS: Forgive me if I'm being slow, but do you therefore expect a transition from low-single-digit penetration today to almost 100% penetration for RTU formats in cartridges over the next 10 years?

PW: Yes.

SS: Do you not see those timelines accelerating in any way because of the breadth and depth of the anti-obesity medication pipeline, specifically GLP-1s [glucagon-like peptide-1s] and combinations of other incretins? Or do you think that transition factors in that?

PW: It's one of the main drivers and there is an expiration date on the patents there, so it can't... any changes need to happen fairly rapidly with the pharmaceutical timelines.

SS: If we think about this 10-year horizon, is it reasonable to say, based on the patent expiry of existing blockbusters, the transition would predominantly be back-weighted?

PW: Yes.

SS: The second half of that 10-year timeline is when we would see the greatest inflection because of patent expiration of major blockbusters?

PW: Yes. It is difficult to make any predictions on what could reduce the pace of transition, but I see the transition itself as inevitable.

[00:06:58]

Q: Just so we have a point of reference, I mentioned that Stevanato assumes less than or equal to 5% penetration for the RTU format in the vial market. What would you estimate to be the penetration of RTU formats in the cartridge market?

PW: Let's make a conservative guess of, start by reaching 50%, where these 50% will be driven by the new types of drugs, including obesity medication.

SS: Forgive me if there's any misunderstanding here. Today, what proportion of cartridges are bulk vs RTU?

PW: I think that it's still bulk.

SS: 90% bulk, 10% RTU, or would you say closer to 5% RTU?

PW: At least 90% bulk. I don't have the exact numbers, but I don't think that the... The last time I checked, the transition hadn't started yet because they are still evaluating the old filling machines that they have used for a long time. These transitions will be driven by building completely new supply lines because that's when you can change the processes and ways of working.

SS: To that point, can these RTU cartridge formats with the apropriate tubs and trays be used with the existing legacy filling machines? Or, do the fill-finish machines need to be upgraded or otherwise replaced before they can cater to these RTU platforms?

PW: That's a very good question. I'm not aware of any restrictions against using because the form factor is the same. It's just the lack of... Well, it included sterility, that is the biggest change.

SS: So the tubs and trays are essentially the same across suppliers? It's simply whether the cartridges themselves are sterile or not, which is the differentiator there?

PW: Yes, but they might... It is a bit speculative, but the cure filling lines might not be in a completely sterile environment, which makes it moot to use ready-to-use cartridges since the environment parameters requires you to sterilise them afterwards anyway. I guess that's the reason why the transition hasn't happened.

[00:10:07]

Q: We have seen the roll-out of certain regulations such as Annex 1 in Europe, which applies the sterile manufacturing of therapies. While a European regulation, I understand this applies to US sites that are supplying Europe. Has the implementation of Annex 1 led to a step change in the number of manufacturing fill-finish lines that meet the sterile requirements for RTU formats?

PW: I haven't been part of any such discussions.

SS: I was just curious to understand whether there was a significant...

PW: That's why I highlighted that my reflections on this point are a bit speculative.

[00:11:02]

Q: The key messaging from suppliers is that an RTU format allows for a faster time to market, lower TCO [total cost of ownership], higher flexibility and so on. Do you think the strength of the value proposition for an RTU platform holds true irrespective of the format, ie, syringe vs cartridge vs vial?

PW: I would say that the benefits are about the same for each format. However, I would also highlight that the ready-to-use vs ready-to-fill is not the main driver when having discussions with suppliers on

the container parameters.

SS: What do you mean by that? Could you elaborate?

PW: I would say that there are at least two other aspects that are far more important than whether it's a ready-to-use presentation. In the short perspective, we have the huge shortage and challenges of getting enough primary packaging, and some aspects of this is that it's often a mix of syringes and cartridges and vials just because of... to acquire as many containers as possible. That leads us to the most important driver, and that is that any supplier need to be able to supply a steady high flow of components.

SS: So essentially...

PW: Essentially, we would accept anything if it was available in a sufficient amount, reliably.

SS: The primary KPCs would be lead times, reliability of supply, and indeed, quantity of supply as opposed to a preference for RTU vs bulk?

PW: Yes. That's by far the biggest driver in the current situation. Then if we move to a longer time span, then we get into the cost and also the shortage of the drug product itself because presuming that we can get enough primary packaging volumes, then we will be limited by how much drug product we can produce. The most discussed aspect there is that the production tolerances in plastics is greater than the production tolerances in glass. On the wish list, when we start becoming limited by drug product supply is a plastic cartridge that can guarantee sufficient lifetime for our drug product.

SS: Do you see value in switching from glass to plastic?

PW: Yes, and the main driver there is the production tolerances that the residual volume would be expected to be lower.

[00:15:02]

Q: Taking a step back and thinking about the value proposition for RTU formats across the different primary packaging categories, we spoke about this prior to the Interview, but cartridges and syringes are considered, at least by the regulators, as pseudo-medical devices, whereas vial is far more of a primary packaging type of format.

PW: Yes, I think it's more of a pharmaceutical container than a device.

SS: Exactly. So, because a cartridge and a syringe is a device, does that mean that this RTU or RTF pre-sterilised format is more or less viable than it would be for a vial? Perhaps an obtuse question, and maybe this is just semantics, but I was curious to understand whether the different definitions had any bearing here.

PW: The typical vial would hold a greater volume than the... Even if it's a multi-dose cartridge or syringe. It's less of a hassle to sterilise those vials yourself, and also the vials will always be considered a temporary solution. What you want to do is you want to provide a ready-to-use, user-friendly solution, and you will never get a vial to become that. While we do accept using vials right now, that's mostly driven by a shortage of supply of other options. If we're stuck with some vials, then sure, it's always

convenient to have sterilised vials, but it's not a terribly important aspect. It's more an availability thing.

SS: Do you expect there to be a greater and faster adoption of RTU cartridges vs bulk cartridges as opposed to RTU vials vs bulk vials?

PW: Yes, because the vials will always be the life raft, so you don't have... you don't spend as much time and energy on it.

[00:17:34]

Q: Could you share a ballpark figure or an estimate for the price difference between an RTU cartridge and a bulk cartridge, and an RTU vial vs a bulk vial?

PW: Unfortunately, my perspective is that of quality assurance and we never ask for costs.

SS: I appreciate this is somewhat in the same vein, but if a customer already has sterilisation equipment in situ for a bulk vial or a cartridge, then does that necessarily mean that going forwards, they will continue ordering bulk primary packaging or do you think there is still an economic advantage to switching to RTU?

PW: I would link that to whether they are planning on expanding their production capacity because if they increase their production capacity, they might not want to increase their sterilisation capacity with that, making it an option to build the new production lines using ready-to-use components so they don't have to expand the sterilisation department.

SS: Do you have a sense for what proportion of CDMO [contract development and manufacturing organisation] or captive manufacturing fill-finish capacity at the market level today has in situ sterilisation equipment vs having to use RTU formats?

PW: No, any answer from me would be too speculative.

[00:19:21]

Q: Let's dig into the supply-demand balance for different formats, starting with syringes and cartridges. You mentioned that, in today's world, the number one KPC is security of supply and available volumes. Could you elaborate on the supply-demand balance for syringes and cartridges today, the lead times and how difficult it is to secure such volumes from the existing suppliers?

PW: Yes. I can just look at how the discussions have changed in the past years, where every discussion around a new supplier used to be whether they can have a lower component price at at least the same quality level. The shift to today's situation where you start asking for any type of supplier that can supply a sufficiently high demand is indicative of a complete and very unexpected per diem shift because that's something that you would never expect the pharmaceutical business to do, since the expectation for, while as long as anyone can remember is that the quality of the components need to go up. Now we're in such a short supply that we start considering, if you reduce the quality somewhat and slack some of the tolerances, can you then provide a higher and more stable supply? We would traditionally never imagine asking that question. As a phenomenon, this indicates that there is indeed a very distinct shortage.

SS: How are lead times trending? Are they extending at all?

PW: I think that there are some projects that haven't been launched because of the issues with securing enough primary packaging and that means that the lead times are large enough that they cause problems.

SS: Would you say the shortage is particularly acute in one format, so a syringe vs a cartridge, or is it equal across both?

PW: It's equal and I think that here, the market is balancing itself that when there is a surplus of one presentation over the other, then you can start using those production lines more until you have a fairly even shortage. With the exception being vials, which we seem to have plenty of, particularly bulk vials, but since no one wants to use those, they are used to fill in the gaps.

[00:22:56]

Q: Given the supply shortage on syringes and cartridges, I understand you're not involved in pricing discussions, but based on what you've heard from colleagues or at industry conferences, are we seeing the suppliers charge a premium for guaranteed volumes, whether RTU syringe or cartridge formats, or indeed the bulk formats?

PW: I have been present when they had those discussions about pricing of the primary packaging. I remember that the cost of these glass syringes was so incredibly small compared to the cost of the drug product that was inside them, so I couldn't remember any more details on the pricing. Yes, from my perspective, then as a QA, there was such a skewness in cost acceptance for the drug product vs the primary packaging that I couldn't absorb any details.

SS: What I'm trying to wrap my head around is, because of the supply chain constraints coupled with the fact that the primary packaging represents such a small percentage of the total cost of the final drug product, are these suppliers essentially able to increase their pricing for the syringe or the cartridges because of this supply-demand imbalance? Do they have price power?

PW: Definitely.

SS: Are we talking a 10% price increase or anything such as that?

PW: I would say more that historically, the department that's been responsible for purchasing these components like primary packaging, they have had, as most departments, their own financial targets that every year they must reduce costs with a certain number of percentages. The biggest difference is that this is not targeted as a KPI anymore since the focus now is exclusively on securing enough volumes. It's not that much that we accept higher prices that we have stopped to aggressively trying to lower prices consistently. This means that if we're not constantly aiming to reduce the price, then there is automatically also an acceptance to raising them, since we monitor this as... It used to be monitored as one of the most important parameters when it came to purchasing primary packaging. Since it's a commodity, you expect the same level of quality from Schott, from Stevanato Group, from Ompi, from Gerresheimer. Since everyone could supply as much as you wanted, then the only thing you could compete with was pricing and that was the only way the procurement department could demonstrate that they were doing a good job because the syringes were all the same.

Now, when we have a shortage, that parameter just isn't important anymore, and it never was that important. It was just important because it was the one thing that they could monitor in that department, and that led to unfortunate situations where we could have a USD 1,000 [sic] worth of drug being packaged on a primary packaging syringe that caused a fraction of a euro. Then we would have the procurement department destroying our relationship with that supplier since their job was to reduce costs of that component. Since that's my background with the whole pricing discussion, I might not be the best person to talk to about component costs.

[00:27:21]

Q: From a QA perspective, are we seeing any decrease in the quality of the primary packaging in exchange for increased volumes?

PW: No, I wouldn't say so. I would say that we've been overspecifying our primary packaging, just because we could, just because we needed some way to differentiate one supplier from another and it wasn't always based on rational requirements.

SS: To be clear, you do not see there being any quality- or sterility-related issues emerging from this supply shortage and scramble to secure primary packaging volumes from the suppliers?

PW: No. The procurement department were guilty of pressing prices, although it strictly wasn't needed because that was the only parameter that they could influence. At the quality department, we were responsible for requiring higher and higher quality. Although, strictly speaking, it wasn't necessary, but it was the one thing we could influence, so we're both equally guilty to different things.

SS: An obvious question, but to confirm, assuming that isn't as significant a bottleneck in the future, is it safe to say that customers would prefer RTU vs bulk formats here as they look to scale?

PW: Absolutely.

[00:29:13]

Q: I understand you're not in the procurement department, but perhaps you've been exposed to such conversations – do you have a sense for how different suppliers are prioritising allocating volumes across their own different customers? How do Schott, Stevanato, Ompi, Gerresheimer and so on prioritise their different customer buckets and determine where the majority of volumes go or who gets priority access to supply?

PW: Yes, I understand the question. I don't have any insight from my position. I hope and pray that they treat their customers equally.

[00:29:53]

Q: Speaking about the cartridge and syringe shortages, do you have a sense for whether the current supply chain bottleneck is likely to resolve itself over the coming months, quarters or years, or do you expect the situation to exacerbate? Do you see syringe or cartridge customers having to switch to vials?

PW: I expect it to become worse, which means that we are preparing in many different ways not to switch to vials, but to use that as a complementary solution to meet market demands where you would have a first-line product that would be the user-friendly presentation in a cartridge or a syringe, but then, also where possible, without inducing risks to the user, also having the vial presentation to meet demands.

[00:31:16]

Q: You expect the supply situation for syringe and cartridges, whether bulk or RTU, to worsen over the near-to-medium term, to the point that syringe or cartridge customers may look to increasingly use the vial format?

PW: Yes.

[00:31:41]

Q: That's a nice segue into understanding the current supply-demand balance for vials, because there seems to be a fairly significant destocking phenomenon for vials, which is to be expected due to the pull forwards in demand due to the pandemic-related vaccines and the subsequent decline in vaccine production over the past few quarters. You alluded to sitting on significant bulk vial inventories. How do you see that inventory destocking for both bulk and RTU vials evolving over time, especially given what we discussed vis-a-vis customers potentially switching from cartridge and syringes to vials?

PW: I would be frank and say that that's not something that we like to think about. We instead hope that the supply... the availability of our preferred solutions with syringes and cartridges, that the availability will increase.

SS: However, if we're being pragmatic, in your view, cartridge and syringe supply chain bottlenecks will persist?

PW: Yes, we will see supply chain bottlenecks. Our potential stocks of vials will run out eventually, but that's a scenario that no one likes to ponder.

SS: How many months of vial inventory are you sitting on today?

PW: No comments.

SS: At the market level, would you be able to give me a sense for how much inventory there is?

PW: I know that we have some inventory and I know that it's not going to last forever, but I can't put a number on when we might run into issues, considering the ramp-up in production and sales that we are anticipating.

SS: To be clear, I'm asking about in the market in general. Do you have a sense for how many months of inventory there are in market for bulk vials? I'd be curoius to understand when we could see an end to the broader vial destocking cycle.

PW: I wouldn't expect more than a year, both because of the increased production and also the tendency

to switch to vials to compensate for shortages in syringes and cartridges. I don't expect the market to have infinite stockpiles, so they can compensate for a while, but I wouldn't expect them to last for that long, but here, we're really at the outskirts of my insights in the primary packaging market.

[00:34:40]

Q: If we look at the recent results from Stevanato, it seems the company underestimated the magnitude of in-market inventories for vials, especially if you look at what management said in its full-year 2023 and Q1 2024 results. Indeed, in the Q1 2024 results, Stevanato disclosed a 43% decline YoY in vials, and that's already following a significant decline in 2023 vs 2022. Why do you think that is? Is there inherently limited visibility in this market for suppliers such as Stevanato or did something fundamentally change from a demand perspective in Q1 for vials that led to an unexpected worsening of demand?

PW: I'm not aware of any specific events. As a trend, I would first expect vials to become less and less appealing as there is an increasing demand for user-friendly solutions, which a vial can never be. In that trend, we go towards a lower and lower fraction of vials, but then we get the unexpected shortage of the preferred solutions, which means that the usage of vial very unexpectedly starts to increase again. The trend for a very long time have been a smaller and smaller use of vials, but the statistics here is a bit difficult because the vials, the syringes and the cartridges, those are all used for liquid drugs. We also have a shift from the classical pills or tablets to these liquid drug product presentations. It's a constant overall increase of all these three, while the relative fractions start tilting to more (? 37.21) the syringes and the cartridges, but as the total volume of these three increase at the cost of the tablets, it's difficult to say which effect that is dominant in the final number of vials sold. It would be a very stimulating, statistical, mathematical exercise to try to rank these effects.

[00:37:58]

Q: When you look at the broader pharma pipeline, the number of therapies that are being developed with an autoinjector – thus requiring a syringe – or variable dose pen – and thus requiring a cartridge – is increasing relative to the number of therapies that require a vial. However, for a therapy that's currently approved and on market in an autoinjector or variable dose pen format, requiring a syringe and a cartridge, respectively, how easy is it to switch over to a vial format? From a QA, QC and regulatory perspective, or even a clinical perspective, what are the hurdles in place there?

PW: Very, very few because using a vial and a syringe for the subcutaneous presentations, you always start with the vial and the syringe. Once you have established the effectiveness of the drug, then you demonstrate that this is not reduced by presenting it on an autoinjector or a pen. The basic data is always there. The one thing that's a potential regulatory issue is that due to health and safety for HCPs, there is an increasing requirement for safety syringes when using vials. These safety syringes, which have the needle shields and some other features, they are themselves medical devices. While you can always have a naked syringe and a vial and you usually have the data to start selling that, straight off the bat, there is an increasing demand for safety syringe solutions, which then requires some paperwork.

SS: Who would you say are the leading suppliers of the safety syringes that could be used in conjunction with a vial?

PW: We have something with an N? Nemera, I think they're called. We had a look at that, and it was

Nemera with their combined needle shield and finger flange and clip-on finger flanges and the plunger rod. I think they were called Nemera.

SS: I'm aware of Nemera.

PW: Yes. They have nice little gadgets.

[00:41:10]

Q: Let's talk about the different suppliers. Stevanato has the EZ-fill platform. However, you have Schott, Becton Dickinson, West Pharmaceutical Services and other players, all of which offer these RTU syringes, vials and cartridges. How are you thinking about the different platforms in the market and whether there are any salient differences across them?

PW: Not really. The only aspect that you sometimes can tell a difference between is the siliconisation. I'm not sure that we have enough data to say for sure that there are any differences between the different suppliers, so I would say that by now, if you go to the RTU segment, the syringes and cartridges, they are commodities. There are no significant differences between different suppliers. As a result, the supplier is selected based on either price, driven by the procurement department, or their quality level, driven by the QA department. That's how it's historically been selected.

SS: To be clear, from a quality perspective, you don't see any material difference across those suppliers?

PW: No. It's mostly a matter of what they put on paper, how large... How small a fraction that they claim could be out of specification.

SS: All Schott, Stevanato, Becton Dickinson, West Pharma and Nemera, all of those are within the usual standard deviation regarding quality. Is that correct?

PW: Absolutely. I have experienced that the different quality levels has been used as a differentiating factor in lieu of anything else being available.

SS: To that point, I appreciate how, in practice, you don't see any material difference in quality, but on paper, is there one supplier that has the best data?

PW: My memory is not very reliable here, but if you press me, then something tells me that Gerresheimer was able to present better numbers at some point, which prompted a shift to them, but I would strongly recommend you to double-check this.

SS: To be clear, any such difference isn't important in today's world when the primary purchasing criteria is availability of supply?

PW: Exactly. Now we're switching from procurement being in charge, selecting them based on price, and QA being in charge, selecting them based on claimed quality levels. Now, it's instead production that is in charge based on the volumes that can be secured.

SS: Which player can provide the greatest volumes or is building out the most capacity in anticipation of providing the most volumes in the future?

PW: Impossible to tell. Everyone can present a good forecast and a good number, but we don't have any reliable data.

SS: To be clear, you have no concern that one player is building out capacity so fast that it isn't focusing on quality or sterility?

PW: Correct. I respect this as a fundamental part of being a syringe or a cartridge manufacturer. Even when they think that they are cutting corners, they're still way, way ahead of the minimum requirements.

[00:45:46]

Q: Based on the corporate material and marketing brochures that are out there, Stevanato claims to be the number one player in RTU vials. Who would you say is the leader in terms of RTU syringe or RTU cartridge platforms?

PW: I don't have any preference there. I see them as equal providers.

SS: To be clear, there's no RTU platform, whether syringe, cartridge or vial, that is more or less adaptable to the broadest range of filling machines, right? Each are equally configurable with their tubs and trays?

PW: They each follow the same technical standards, so by necessity, they need to be very similar.

SS: To confirm, there's no one player that is most flexible?

PW: No. They are both equally supported and hampered by the technical standards.

SS: When you say hampered by the technical standards, what do you mean by that?

PW: You can't offer a new and groundbreaking design as this would not be permitted by the standards for dimensions of primary packaging, which ensures that a big pharmaceutical company can easily switch between different suppliers and they can easily compare quality levels between them, which is the whole purpose of standardising this, but this also prevents them from potentially offering something groundbreaking.

SS: Which propagates the commoditisation pressure you highlighted earlier?

PW: Exactly, yes, and the commoditisation pressure is, you have the accumulated pressure from decades of standardisation.

[00:47:56]

Q: We know Stevanato has a fairly large engineering business insofar as it actually ships and installs fill-finish lines. Do you think that vertical integration, which is seemingly fairly unique when you look at the competitive landscape, serves as any differentiator or driver for customer spend?

PW: I would say that those initiatives that can make a difference.

SS: However, in this instance, given the supply-constrained environment, the fact that Stevanato can install a fill-finish line doesn't move the needle? Or does it?

PW: When you have Stevanato who can do the filling lines, getting it more contacts, more interactions with the customer, you have Schott that have a very good lab for analysing syringes, you have West who supply the rubber plungers. All of those add-ons, of course, increase the number of contacts between you as a supplier and the customer, which is an advantage when you try to expand your business. Everything else equal, like in the good old days, when it was a commodity, the quality level was the same, the price was about the same, everything was standardised, then this was the only leverage you could find. Now, we're in a situation that the first supplier that can reliably increase the production levels will have a huge advantage. This would work twofold. First, they would make more money, because they would sell more components, and they would also be selected because they could sell more components.

[00:50:08]

Q: I'm not too familiar with West Pharma, but if you look at the company's range of products, it seems to offer a robust portfolio of plungers and stoppers. Whereas, if you look at Stevanato's products, they're far more indexed to the glass primary packaging component itself. In a normalised supply environment, is West Pharma offering a complete product portfolio including plungers or stoppers is more of less of a differentiator? As a customer, do you select the best vendor for the glass primary packaging, the best vendor being selected for the plungers and stoppers and so on? Ie, is this one-stop-shop component as valuable as it may seem on paper?

PW: It's difficult to tell because having more components and more interactions, for sure, we had a lot of extra discussions with West on a project because they could supply the finger flanges and the plunger rods for our clinical studies, and they also have the lab. As it were at the time, the only two deciding factors were the component costs and the documented quality level have... Those are two so objective properties, but it's very difficult to compete against them with these very, very non-quantifiable aspects. You want to think that they would have an edge, but I think that the boring answer is that at the end of the day, it boils down to these quantifiable aspects, since people don't have anything better to do than to find something quantifiable and then base the entire decision on that, regardless of whether it makes sense.

SS: What I'm still struggling to understand is if there are any quantifiable differences between the players. In principle, I understand these aren't material, given all of these primary packaging formats are standardised in such a way that they can be considered interchangeable. Yet, you have suppliers that are emphasising that their products or services have proprietary IP. They offer something that is unique and differentiated. Stevanato claims to have this IP and proprietary know-how. What exactly is it? What can it do that other player can't? Is there anything to do with the washing, siliconisation, sterilisation or traceability that really makes Stevanato the go-to in a normalised supply environment, or is there any one player that stands out at having that quantifiable edge?

PW: No. There is currently no quantifiable edge. It's sad because you want companies to be rewarded for ingenuity and focusing on development, but there's not a lot you can do in this highly standardised, highly regulated market. Then again, now we have created different situation where no one cares about these old metrics anymore, but only asks, "So, how much can you supply, and how can we be confident that you can keep up this supply?"

[00:55:00]

Q: Interestingly, Stevanato sterilises its syringes in-house, whereas Schott outsources to a third-party CDMO. If I had to guess, I'd assume someone such as Steris, for example…

PW: If you have to pick one guess, that would be the one.

SS: Yes. Is that a key differentiator that would drive customer spend? For you, as a QA professional, are you concerned that Schott outsourcing to a third-party CDMO could lead to worse quality than Stevanato or indeed, are you assuming the opposite, given the pedigree that a player such as Steris may have?

PW: I would never see it as a factor either way because in our quality agreements, one of the most important aspects is that the supplier demonstrates that it has control of its own suppliers. Once they have demonstrated that they have control of their own suppliers, then they will always have suppliers, then we don't care which aspects that are outsourced and to what extent. We only want to see that they demonstrate a robust process, and what all these have in common is that they are extremely good at quality agreements and supplier control.

SS: Based on your conversations with the procurement department, you don't believe that such use of third-party value chain players is a limiting factor? You don't think procurement departments are looking at the fact that there's an additional value chain player here with Schott as an additional layer of complexity that could impact their ability to supply?

PW: No, because there have never been any indications that these suppliers of sterilisation services have been unreliable.

[00:57:13]

Q: Going back to the lack of differentiation across players, I'd like to circle back to an earlier comment you made regarding the use case of polymer vs glass. Could you walk me through the value proposition of glass vs polymer, whether COC [cyclic olefin copolymer]- or COP [cyclic olefin polymer]-based primary packaging, and which supplier you think is the leader in the polymer syringe or cartridge market?

PW: The value-adding aspect is that the tolerance… the precision of polymer primary packages is greater than that of a glass container. As an effect, you would expect a lower residual drug product volume, which in turn means that if you're limited in how much drug product you can manufacture, which will very much be a situation for a very long time for several blockbusters, then a polymer primary packaging with the lower residual volume would mean that you can sell more devices.

SS: When you say lower residual volumes, are you referring to the volume of drug product left in the primary packaging container after the dose has been delivered?

PW: Correct, which then influences the amount of overfill that you need to have in that primary packaging.

SS: Is there a rule of thumb for the extent to which using plastic over glass would lower the residual drug product volume? Does this save by 10%?

PW: Not really. It's more that it's inherent to all glass syringes, that they will have a higher residual volume than a polymer one. It's not that important how large this is since it's systematic, and everyone knows that this could be eradicated almost completely with a polymer product.

SS: With no particular reference to a particular drug, in general, if a pharma customer were to shift an injectable drug from a glass syringe to a polymer syringe, by how much in would that reduce the total API [active pharmaceutical ingredient] one would have to manufacture per dose?

PW: At least several percent.

SS: Perhaps low-single-digit percentage points?

PW: Yes.

SS: The fact remains that it seems polymer as a packaging format has been discussed for a number of years now, but...

PW: There have been so many, so expensive projects.

[01:00:19]

Q: I'm not sure I understand how much traction polymer is actually getting, and over what timelines we could eventually see the switch from glass to polymer. I understand that polymer has some advantages, but as you say, there have been many projects that have fallen by the wayside. Do you see a concerted shift away from glass and towards polymer at the market level anytime soon?

PW: First, we need a proof of concept. We need a product that demonstrates that you can maintain the two years' lifetime in this polymer primary packaging that you would have in a glass container. There have been... I don't know the name of the supplier, but I've heard that there is one supplier who has provided a polymer container that was treated on the inside to give it a glass-like surface, if it was some fancy plasma treatment and that treatment... There were indications that this extended the lifetime of the drug enough. If this can be established that there is at least one supplier that can provide a polymer syringe with the sufficient tolerances that is treated on the inside to provide sufficient lifetime for the drug, then it becomes, very quickly, a comparative exercise between the added cost for that primary packaging container and the reduced cost for the overfill of the drug product.

SS: To be clear, that critical dataset has not been built out yet?

PW: No, but there are... We were going from no indications that it will exist to some indications.

SS: I suppose it's better than nothing.

PW: It's really nothing, and since it's the golden goose that everyone's been chasing for quite some time.

SS: Is there one player that really stands out to you as having the most commitment to this glass-to-polymer transition?

PW: Yes, I've heard that there is supposed to be a supplier that is the only one who has provided a promising solution.

SS: Who is that?

PW: That's the thing. I wasn't able to collect that information. I mean, no one was that interested during the discussion. As engineers and quality personnel, we were more interested in the technology itself and whether they could make this feasible than the name of the company.

[01:03:32]

Q: Do you think the shift to polymer is the solution to offsetting the commoditisation pressures we're seeing in glass primary packaging?

PW: Sure. If you can provide a polymer solution that's only marginally more expensive than the glass solution, then you have the first opportunity in a very, very, very long time to differentiate yourself in this market.

[01:03:58]

Q: Specialists in previous Forum Interviews have argued that Schott is the market leader for polymer syringes. Do you know much about what this company can bring to the table from a polymer standpoint?

PW: I don't have enough confidence to confirm whether Schott was the supplier that was mentioned here with the experiment. It could have been mentioned in passing, but it might also be something that I just made up. Since as a QA, you don't pay that much attention to these specific suppliers. Another aspect is the existing filling machines. In the good old days, they weren't adapted to the polymer syringes because they weren't heavy enough, but with the recent updates to the filling stations, they are being built so that lighter polymer syringes could be used if this problem is ever solved. There are preparations being done within the pharmaceutical industry.

SS: Interesting, but to be clear, that's only for the newer fill-finish lines that are being brought to market?

PW: Yes, it's for the newer ones, but since they will usually have a lifetime of several decades and everyone is now sufficiently optimistic that they spend the extra money on adapting them for the not-yet-existing polymer syringes.

SS: Could you retrofit legacy filling machines to accommodate these lighter polymer syringes or would you have to replace it with a newer line?

PW: I think we would then need to replace it because the process validation would be such an undertaking that the additional cost of getting something new and reliable would be that high.

[01:06:06]

Q: If we think about the GLP-1 [glucagon-like peptide-1] opportunity for primary packaging suppliers, at the market level, do you get the sense that the obesity market in the US will move away from autoinjectors and thus syringe platforms and increasingly towards variable dose pens and thus

cartridges, given the titration needs for these GLP-1s? I believe the European market does use cartridges and pens already.

PW: Yes. Generally speaking, a drug... a treatment regime where you have a fixed dose that is a fraction of the filling volumes of the traditionally-used cartridges, say that you have a fixed dose of 0.75millilitres, and you traditionally use 3millilitre cartridges, then it's very close to imagine a multi-dose device, similar to what you have for the insulin pens, but the difference in this case would be that if you don't have a variable dose, which we very much have in insulin, that its users have its own specific dosage and that's why you have the selection wheel. If you have a treatment where you have the same dose to all patients, then you don't need this dose selector, but it would still make sense with a multi-dose bolus device.

SS: To confirm, you don't see the pendulum swinging all the way to the insulin variable dose pens where you have this selection wheel, but you do see a movement away from the autoinjector platforms to a cartridge-based systems where on the same device, you can have multiple different doses?

PW: You would switch cartridge every now and then, and you would switch the device every couple of years.

SS: Which obviously has added ESG benefits, and those are clearly a priority at the moment.

PW: Yes. That's one of the main drivers to reduce waste as much as possible, and that's also one of the aspects of using a polymer primary packaging to have the entire thing recyclable.

SS: What about dual chamber syringes?

PW: Dual chamber syringes are good whenever you have a drug product with a short lifetime.

[01:09:10]

Q: We know certain pipeline GLP-1 therapies use dual chamber syringes. However, is this simply a stop-gap while co-formulation is refined. I'm curious to understand whether the market as a whole – from a patient convenience, regulatory and QA and QC perspective – wants to move away from dual-chamber- to single-chamber-device platforms, or whether you think the market is happy to accept the dual chamber technology for the foreseeable future. What are your thoughts there?

PW: Generally speaking, the dual chamber is the emergency temporary solution, the same way as vials is, where you would rather use a single chamber platform, but you're forced into dual chamber because of drug product properties. If you could modify those drug product properties to allow for a single chamber device, you would do that every single time.

[01:10:28]

Q: Is there anything we haven't discussed today or that you would like to underline around primary pharmaceutical packaging?

PW: No, I think that we have covered the most ground where traditionally, there haven't been any differentiation between the major suppliers of primary packaging. Currently, the main differentiator is

in production volumes. In the future, we might see differentiation based on the availability of polymer primary packaging.

SS: I think that's a very good note to end the Interview on, Peter. Let me close by saying thank you very much for your input. Clients, thank you as well. For now, everyone, have a wonderful morning or afternoon. Peter, thank you again, sir. Take care.

PW: Thank you.

SS: Cheers. Bye-bye.

Transcription ends at 01:11:34 of the recorded material

If you'd like to speak to Peter Wengström in a private call or meeting, please let your relationship manager know.