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Market Entry and Positioning for the Drug A Manufacturing Services Space – Strategic Analysis Reporting for Company X

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Market Entry and Positioning for the Drug A Manufacturing Services (PDMS) Space – Strategic Analysis Reporting for *Company X*

Executive Summary

A value chain analysis conducted on *Company X* (in hereinafter the "client") revealed the combination of activities to be initiated within its value chain in order to gain competitive advantage in the *Drug A* manufacturing services (PDMS) space. An organization structure was proposed for the client based on the model of each value chain operating as a strategic business unit (SBU). The client's packaging production infrastructure needs to transform from manual to continuous automated production lines in order to deal with the high capacity units of package production needed in this high demand growth segment of healthcare packaging. This infrastructure should also incorporate just in time (JIT) and continuous improvement (CI) elements in manufacturing single use system (SUS) packaging components. As this is a new market entry initiative, the client's human resource management are required to hire experts from stable sterile formulation design, sterile packaging QC, cGMP specialist areas as well as industry leaders in sterility material science, process engineering & production technology. As SUS is a staunch growth area in the PDMS space, the innovative packaging technologies SBU of the organisation are tasked with designing and developing SUS solutions that meet component compatibility, scalability, sterility, biocompatibility, eco-sustainability, hybrid systems & quality-by-design (QbD) flexibility needs and to incorporate unique technology features in those packaging products. Owing to the competitive and dynamic nature of the PDMS space, the procurement of primary packaging material SBU of the company is required to have high-tech. procurement systems in place deriving cost savings, process improvement, supplier innovation, optimum price negotiation & contractual terms to gain the needed competitive advantages. The client's value chain was further scrutinised for potential value chain linkages both in terms of co-ordination of linked activities and integration of activities, the details of which are described in Deliverable 1 of this report. Finally in Deliverable 1 by comparing the value chain activities and drivers for a low cost strategy with a high value differentiated (HVD) one, the key drivers for the HVD strategy will depend on the client's service quality and level, product features, delivery times and the company image it upholds in the PDMS space.

In the next deliverable, *Porter's Five Forces Analysis* was used to describe the macroeconomic variables affecting aggregate demand and therefore the external competitive nature of the PDMS space globally. Whilst the threat of new entrants and the bargaining power of raw material suppliers in the PDMS space was recognised as being low, the element of competition is coming from the threat of packaging product substitutes and the high bargaining power of biopharmaceutical manufacturer buyers of *Drug A* packaging material. A further examination of the low and high profitability scenarios using Porter's Five Forces was presented, and the client is urged to focus on those critical factors which will yield high profitability as outlined in more detail in Table 4 of this report.

In Deliverable 3, upstream to downstream HVD products were assessed for their rationale in selection and the client's transfer capabilities (from the client's current medical device product and service portfolio), client's change requirements, market profitability and stopgaps were also evaluated. For single-use bioreactor media containers, the transfer capability is low, whereas the profitability is high. Stopgaps cited for this product are: gaining marketing approval, acquiring validation of compliance and acquiring the necessary global logistics and distribution networks. For ready-to-fill and port bag containers, these products represent both a high transfer capability and

profitability for the client with stopgaps of biocompatibility, acquiring marketing approval and validation of compliance. Clean rapid transport ports (CRTPs) are noted as a medium transfer capability opportunity but with low profitability furthermore there are stopgaps of low return on investment, along with marketing approval and validation of contamination control challenges. Closure processing systems (CPS) represent a low transfer capability yet a high profitability. Stopgaps noted are: stringent physico-chemical and biological testing required to meet sterility and safety standards and acquiring marketing approval. DPTE (in French: Double Porte pour Transfert Etanche) beta containers were revealed as a low transfer capability and medium profitability product with stopgaps of: the design of the container to cope with high productivity targets, production throughput and hence in transfer operations; the stringent security (interlocking between isolators/restricted access barrier systems (RABS)) requirements, both for the transfer port user and for the transfer itself; greater emphasis on ergonomics, driven by the evolution of labour legislation around the world to protect operators from musculoskeletal disorders. Glove leak and transfer leak testers (GLTs & TLTs) are low transfer capability but high profitability products, with the stopgaps being: stricter preventative maintenance programs and new glove or sleeve (gauntlet) assembly technology being introduced impacting on lower leak incidences; the choice of durable glove materials, coupled with a well-justified replacement frequency, are key aspects of good manufacturing practice and thus in principle minimises the need for GLTs & TLTs. Isolators would be a low transfer capability and medium profitability market for the client with stopgaps noted as: biopharmaceutical manufacturers switching to RABS due to affordability and flexibility; RABS could replace the more cumbersome vaporised hydrogen peroxide (VHP) isolators and can deliver significant time savings to certain parts of the PDMS space, speeding up the manufacturing process and offering the flexibility. Aseptic prefilled syringes are a high transfer capability product opportunity for the client albeit deriving low profitability. Stopgaps for this product are: the numerous key providers in this segment;
Certain *Drug A* require small filling volumes and this creates an increased demand on all production areas, including process design, technical equipment, and packaging material. Transdermal patches and on-body devices and implantables represent low transfer capability yet high profitability products. The stopgaps are: a long anticipated regulatory approval timeline and the patient training and education requirement as an additional logistical and cost hurdle. In this deliverable also the critical success factors for the client to become a "market winner" were also delineated and these were: flexible packaging and development, providing an automation solution, implementing single-use systems as a packaging solution, implementing QbD elements into the packaging products and developing patient-centric packaging solutions.

In deliverable 4 *strategic group analysis* was used to identify the ways in which particular groups of companies compete to provide product and services to SUS drug manufacturers. The key to this approach was to identify three or four sets of characteristics that seem to establish key differences between the companies competing to provide product and services to SUS drug manufacturers. The following sets of competitors were found to offer respectively their strategic set of product and services to SUS drug manufacturers: *Company Y* & *Company Z* – offers SUS packaging to cater for buffer solutions and cell-culture media production; *Company S* & *Company W* – provides SUS packaging for end to end scalability; *Company Z* & *Company W* - offers SUS packaging compatibility between single-use systems; *Company S* - packaging accommodates for hybrid process design; *Company S* & *Company Y* - SUS packaging demonstrates end to end biocompatibility; and *Company S* – has acquired validation status as an SUS packaging supplier.

For deliverable 5, feasibility studies were conducted on ultraclean, rapid prototyping, material & design expertise and trouble-shooting services, each service representing a case study as to whether it would be feasible to develop such a service as a SBU. A step-wise approach was performed using research findings from key market leaders in the PDMS space who offer such a service. Feasibility was graded high, medium or low from the client's perspective of its current operational and financial position. All services were graded as medium feasibility as a SBU in the PDMS space with the exception of material & design expertise that was assessed as a high feasibility SBU. As positive as these outcomes appear however, upon access being granted to the client's financial statements, these findings should be analysed for further refinement and recommendations put forward accordingly.

Deliverable 6 gave a go/no-go analysis on the HVD product offers in the PDMS space. This was a holistic approach whereby the strategies for new-product screening was based on four criteria: 1) customer's values, expectations and requirements, 2) competitive situation and trend 3) company's goals and competitive strategies and 4) technological opportunities, and company's capabilities and resources. In assessing the viable and profitable new product ideas, the following three criteria were used: 1) right product features and characteristics, 2) right time to develop 3) right amount of development investments. Although the outcome of this analysis for the development of CRTPs, CPSs, DPTE beta containers, GLTs & TLTs and Isolators were *all no-go*, upon access being granted to the client's financial statements and financial planning reports, these findings should be analysed for further refinement and recommendations put forward accordingly.

The retro-analysis (from the lowest downstream point, e.g. *Drug A* administration to the patient to the highest upstream point of the process, e.g. bioreactor mixing in this order) reporting in deliverable 7 identified blind spots, stopgaps and value chain improvements at each stage of the *Drug A* packaging process. In-depth value chain improvements have been proposed to the client as highlighted in Table 9 of this report. Key blind spots cited for each stage of the *Drug A* packaging process were as follows: finished products - counterfeiting, child-tampering, marketing myopia and patient compliance; in-process - human operation, marketing myopia, perceived low importance of quality control (QC) and validation processes; assembly stages - bioreactor packaging not amenable to hydration and rehydration processes and lack of long term storage capability in the assembly packaging.

In deliverable 8, negative influences or "disruptors" were identified for each of the six macro-business factors – political, economic, social, technological, legal and environmental in the PESTLE analysis for both in the 3-year short term (2022) and 10-year longer term (2029) in the PDMS space. In the short term, the key disruptors will be: political – a no-deal Brexit; economic – rise of packaging material prices imported from/exported to China until a new US-China trade agreement can be ratified; social - raised consumer expectations regarding packaging formats and features; technological – *Drug A* manufacturing demanding fast changeovers between different packaging containers with robotic control the only way to cope with this production design; legal – a large volume of bio-generics and bio-similars impacting on regulatory authorities to impose stricter cGMP guidelines; environmental - pressures from environmental lobbyists to justify the high turnover of raw materials needed in SUS based *Drug A* manufacturing and packaging.

From the reporting of deliverable 9, the key markets and products needed for heightened focus in the PDMS space are: HVD packaging products for SUS based biopharmaceutical

manufacturers, on-body devices and implantables, HVD packaging products offering flexibility, scalability and assured sterility of *Drug A* manufacturing, incorporation of smart raw material into the packaging products to meet the bio-compatibility, bio-burden, leaching and sterility challenges and acquisition of strategic partnerships with pharma and contract development manufacturing organisations (CDMOs) for sourcing of appropriate raw materials and the final packaging formats.

Finally deliverable 10 presented some high-level market survey results. The global revenue from the sales of *Drug A* packaging products is estimated to exceed $16 billion by 2028. The current global share of injectable drug delivery systems and transdermal drug delivery systems segments represent collectively 30 to 40% of the total novel drug delivery system (NDDS) market revenue share. The global transdermal drug delivery market will continue to accelerate at a >4% CAGR to 2023. India is a high potential emerging market with a therapeutic injection segment of the large volume *Drug A* market worth $29 million by 2024. The pharmaceutical *Drug A* containers packaging market in North America will reach a revenue of $4.98 billion by 2021.

i3 Consult's Pledge of Affordable Quality Delivered

Unlike the blue chip consulting firms, our fees are very competitively priced and are based on the deliverables you require. Our deliverables are from dedicated specialists and experts in the healthcare and life science industry rather than from new graduates and mid-career hires of the big consulting firms and we do not charge by the hour but more by the scope and critical need of the consultancy required. After assessing the content of this report, please tick off the checklist (Table 1) boxes (☐) below if you are satisfied with our delivery. Of course with any boxes left un-ticked, we will be prompt to follow up on the reporting action required. Only priority one (1) deliverables are in included in this copy. In the final report, with both priorities (priorities 1 and 2) deliverables presented, an executive summary and take home points will be included.

Table 1: Checklist of Deliverables for the Client

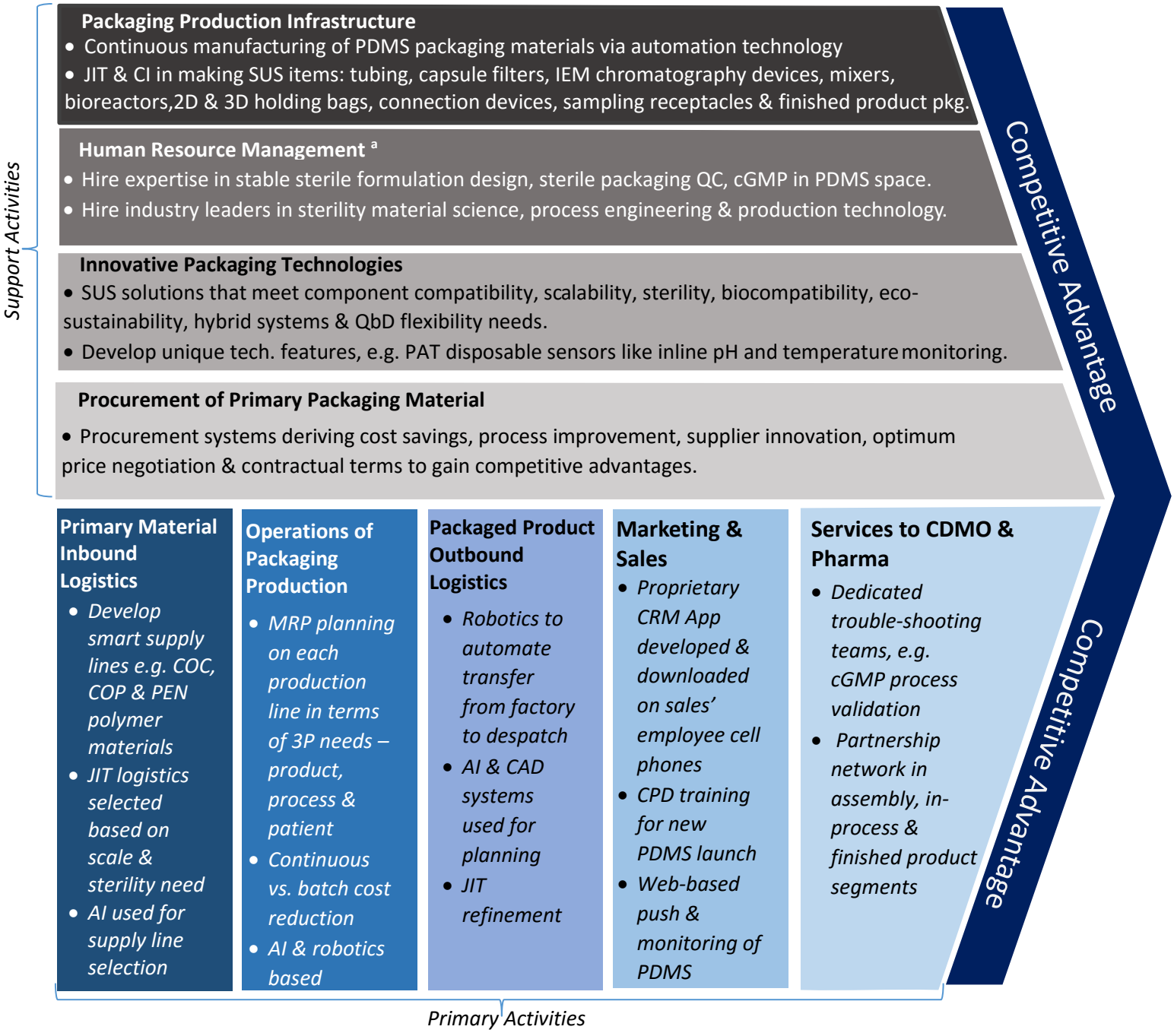
Ref	Description	Priority[1]	Page No.	Tick (☑)
1	Value Chain Analysis	2	7	☐
2	Porter's Five Forces Analysis	1	10	☐
3	Define product offers within PDMS space that align with all key market influences and *Company X* 's interest to provide high value, differentiated solutions. Include requirements needed to win within that space.	1	13	☐
4	Complete a market assessment of competitors who provide product and services for SUS manufacturers	1	28	☐
5	Feasibility case studies of ultraclean, rapid prototyping, material & design expertise and trouble-shooting services. Define what *Company X* needs to offer to win in PDMS space.	1	32	☐
6	Go/No-Go analysis on development of DPTEs or Clean Rapid Transport Ports (CRTPs), Closure Processing Systems (CPS), DPTE beta containers, Glove Leak Testers & Transfer Leak Testers (GLTs & TLTs) and Isolators.	1	34	☐
7	Retro Analysis Reporting (from the lowest downstream point, e.g. *Drug A* administration to the patient to the highest upstream point of the process, e.g. bioreactor mixing) identifying blind spots, stopgaps and value chain improvements focusing on a reduced product development timeline, reduction in costs of labour, material and utilities, increased process efficiency, increased productivity, and reduced risk of cross-contamination.	2	37	☐
8	Potential Disruptor Reporting – Use of the PESTLE framework approach to identify disruptors, 3 and 10 years onwards.	2	45	☐
9	Identify any key market/product for heightened focus and why.	Optional	48	☐
10	High level reporting on Market Size and Share from in-house data available.	1	49	☐

[1] Priority 1 Deliverables due Tuesday, July 30th; Priority 2 Deliverables due Tuesday, Aug 6th

Deliverable 1: Value Chain Analysis

Companies rarely create competitive advantage as a result of one value chain activity. Indeed, were the client's organization to rely on such an activity, it would be at risk of losing its competitive advantage, as particularly in the face of the highly competitive nature of the PDMS space (see Deliverable 2), its competitors would find it relatively easy to replicate the activity within their own value chains. Hence Figure 1 highlights how the client can create competitive advantage through a combination of activities within its value chain. Also Figure 1 represents a re-structuring model for the client's organization. Each value chain activity could potentially be developed into a strategic business unit (SBU) within the client's organization.

Figure 1: *Competitive Advantage Created for the Client by a Combination of Activities within its Value Chain*



[a] Further hires: Production supervisors to assure sterile, timely, efficient manufacture; HR structure to coordinate Maintenance, Engineering, QC & QA responsibilities of production; Floor managers lead scheduling, maintenance planning and provides key leadership for production staff

Value Chain Linkages A key aspect of organizations is the interdependence or linkages between their various activities. Whilst value activities are the building blocks of competitive advantage, linkages also can lead to competitive advantage in two ways:

- Co-ordination of linked activities such as procurement and assembly can reduce the need for inventory, for example. Reducing inventory is made possible by managing linkages better.
- Integration of activities can create the opportunity to lower the total cost of the linked activities or increases the value added. In *Drug A* manufacturing, for example, patient compliance of the drug is linked to the technology elements integrated into the packaging to ensure that it is a patient friendly experience during self-administration.

Table 2 highlights some of the potential value chain linkages for the client both in terms of co-ordination of linked activities and integration of activities

Table 2: Potential Value Chain Linkages of *Company X* based on Co-ordination of Linked Activities and Integration of Activities

Co-ordination of Linked Activities	Integration of Activities
• JIT of both inbound and outbound logistics of packaging raw materials and finished products coordinated to minimize inventory floor space. • A corrective feedback loop needs to be set up between the Services to CDMO & Pharma SBU and the Innovative Packaging Technologies SBU (see Figure 1), to ensure R&D strategy and operations are aligned with immediate and ongoing customer needs • Human Resource Management SBU needs to periodically survey Innovative Packaging Technologies SBU for its information updates, training and continuous professional education needs e.g. attendance at international conferences and forums, so as to keep up to date with cutting edge technologies and advances in the PDMS space to enable them to apply it to projects they are working on or are planning for in the future. • For cost and time reduction savings, a monitoring system to be set up between the Procurement of Primary Packaging Material SBU and Innovative Packaging Technologies SBU to eliminate unnecessary purchases of components which can be developed and manufactured internally in a cost effective manner.	• Product R&D teams need to resolve the child-resistant vs. senior-friendly packaging paradox. For finished products, the need for child-resistant packaging can conflict with senior-friendly packaging. R&D must integrate their efforts to resolve this paradox, creating a package that children cannot open but older adults can. • Integrate polymer technology/material science into primary packaging, which control moisture, oxygen and other gases that can affect the stability and shelf life of the active pharmaceutical ingredient (API) biologic, while minimizing product impurities. For example CSP Technologies Inc. can injection-mold their polymer technology into components for drug delivery devices (e.g. large-molecule transdermal drug delivery systems) and can extrude the technology into a film that can be heat-staked onto foil substrates to absorb moisture and oxygen to protect transdermal patches • Integrate material science expertise in a theoretical, analytical and practical application approach in solving the solubility and diffusion challenges in the packaging of *Drug A* biologics and excipients. • Innovative Packaging Technologies SBU to audit existing product portfolio and to

	create designs that integrate the organization's existing proprietary technologies e.g. Transfer Port Isotech® Bags into product development streams for market release into the PDMS space.

Choice of a Low Cost Strategy vs. High Value Differentiated (HVD) Strategy
The value chain offers a systematic model for the client that can be used to examine the activities its organization performs and how they interact in order to identify and develop existing and potential sources to gain competitive advantage in the PDMS space. By performing some activities better than the competition, or creating linkages between activities, the client can either increase value or reduce overall costs, both increasing the margin available to the firm.

In other words, *Company X* can create its generic strategy through the activities and linkages of the value chain cited above. The idea is to identify all the potential sources of competitive advantage - either cost drivers or differentiation drivers - and exploit them within the company. Some of the potential activities and sources of advantage are outlined in Table 3.

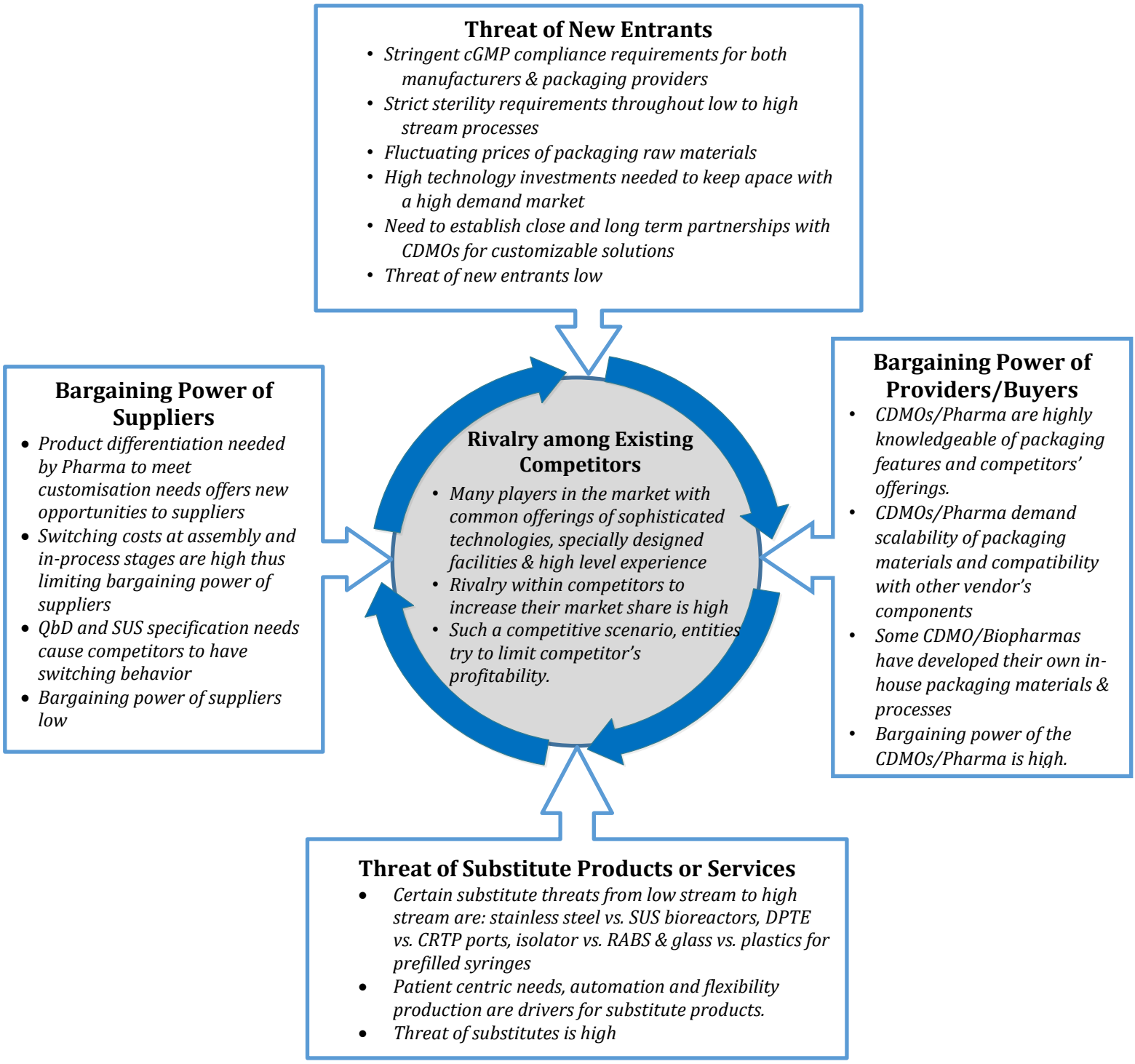
Table 3: Potential Activities and Sources of Advantage for a Competitive Advantage

LOW COST STRATEGY	**DIFFERENTIATION STRATEGY**
Critical Activities • Efficient Operations • Low cost logistics & distribution • Process design – efficient processes • Product design – easy to make products • HRM – good labour supervision	**Critical Activities** • Product design – innovative products • Marketing – brand image promotion • Service – quality customer service • HRM – staff training • Operations – quality assurance
Cost Drivers • Economies of scale • Economies of scope • Experience curve • Supply costs	**Differentiation Drivers** • Service quality and levels • Product features • Delivery times • Image

Deliverable 2: Porter's Five Forces Analysis

The PDMS space that has a very strong position in the major global markets – North America, Europe and APAC regions, commanding a relatively high share of GDP and therefore represents one of the most competitive segments in the healthcare industry. A starting point is the analysis of the external environment using *Poster's Five Forces Analysis*, describing the selected macroeconomic variables affecting aggregate demand and therefore the PDMS space globally (Figure 2).

Figure 2: Porter's Five Forces Analysis of the PDMS Space



The PDMS market can be described as highly competitive, with a large number of small and medium-sized companies, stable innovative activity, which is significantly defined by cGMP regulations as stipulated by the respective regional authorities. Globally, this industry has been growing stronger year on year and will change pace to exponential growth in the next five years.

The ultimate strength of competition in the PDMS depends on the collective strength of the forces illustrated in Figure 2: sometimes one will dominate; often it's a collection of 2 or 3. To understand which of these forces is likely to be most significant means investigating the structural factors that underpin them. A summary of the critical factors that could influence the forces of competition, affecting the profitability of the PDMS space and the competitive advantage of companies within it are outlined in Table 4. **Therefore in its planning and execution of its HVD strategy in the PDMS space, the client is urged to focus on those critical factors that will yield high profitability.**

Table 4: Critical Factors Affecting Competitive Advantage in the PDMS Space

	Will Lower Profitability	*Will Raise Profitability*
	Easy to Enter	*Difficult to Enter*
Ease of entry	*> Low scale threshold* *> Little brand franchise* *> Common technology* *> Access to distribution channels*	*> High scale threshold* *> Brand switching difficult* *> Proprietary know-how* *> Restricted distribution channels*
	Difficult to Exit	*Easy to Exit*
Ease of exit	*> Specialised assets* *> High exit costs* *> Interrelated businesses*	*> Saleable assets* *> Independent business*
	Suppliers Powerful	*Suppliers Weak*
Power of Suppliers	*> Credible forward integration threat by suppliers* *> Suppliers concentrated* *> Significant cost to switch suppliers*	*> Many competitive suppliers* *> Purchase commodity products* *> Credible backward integration threat by purchasers* *> Concentrated Purchasers*
	Customers Powerful	*Customers Weak*
Power of customers	*> Buyer concentrated* *> Buyers purchase a significant proportion of output* *> Buyers possess credible backward integration threat*	*> Producers threaten forward integration* *> Significant buyer switching costs* *> Buyers fragmented* *> Producers supply critical portion of buyers input*
	Substitution Easy	*Substitution Difficult*
Availability of substitutes	*> Low user switching costs* *> Substitute producers profitable and aggressive*	*> Higher user switching costs* *> Substitute producers unprofitable and passive*
	Many Competitors	*Small Number of Competitors*
Industry Conditions	*> Competitors equal in size* *> Slow demand growth* *> High fixed cost* *> Excess Capacity* *> Commodity products* *> Diversity of approach and historical background*	*> Diversity of competitor size* *> Industry leader* *> Fast demand growth* *> Low fixed cost* *> Differentiated products* *> Commonality of approach and historical background*

Deliverable 3: PDMS Products Offering HVD Solutions and the Critical Success Factors to be a Market Winner

Since we have seen a 5-year on year exponential rise in the number of biopharmaceutical investigatory new drugs (INDs) submitted to the FDA with no indication of a slowdown, the global *Drug A* packaging market is forecast to experience significant growth. In findings by *Market Research Company M*, this market was valued at $8.69 billion in 2017. By Q4 of 2024, however, the *Drug A* packaging sector is estimated to be valued at $18.2 billion with a compound annual growth rate (CAGR) of 11.14%[2].

The legal regulatory framework in cGMP, in particular in the FD&C Act Section 501(a)(2)(B) is to be noted:

"A drug shall be deemed to be adulterated if the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirements of this Act as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess."

Drug A therapies, necessitate ultraclean and sterile processing from development to fill or finish. Regulatory bodies demand full inspections for visible particulate with specifications for *essentially* zero particles for injectable drugs. Thus it is a high cost and therefore represents a high value market segment. In-process packaging necessitates the transport and aseptic transfer of key components into RABS and isolator equipped facilities. Developments in micro-needle, transdermal & intradermal drug administration systems as alternative routes of drug delivery are pushing additional therapy applications. Segments within each of these target markets will require barrier packaging solutions to protect from moisture and UV to preserve treatment formulations and extend shelf life. Aseptic processing and packaging of *Drug A* poses a number of product and service development opportunities for the client, including:

- Protecting the sterility of the product as it moves through several phases of formulation, filtering, filling, and packaging.
- Development of the experience and technical knowledge to trouble-shoot issues as they occur.
- Maintaining consistent compliance with cGMP regulatory requirements to protect product safety, integrity, strength, purity and quality (SISPQ).

In Table 5, the present HVD product offerings in the PDMS space are evaluated for strategic rationale, transfer capabilities (from the client's current medical device product and service portfolio), client change requirements, profitability and stop gaps.

[2] https://globenewswire.com/news-release/2018/09/04/1564617/0/en/Global-Parenteral-Packaging-Market-Will-Reach-USD-18-20-Billion-By-2024-Zion-Market-Research.html Accessed July 2019.

Table 5: Evaluation of Present HVD Product Offerings in the PDMS Space

	HVD Product	Strategic Rationale	Transfer Capabilities	Client Change Requirements	Profitability	Stop Gaps
Assembly Products	Single-use Bioreactor Media Containers (SUBMC)	The Single-use Bioreactor Market is expected to grow at a rate of 15.5% over the forecast period, 2018 to 2023. The development and formulation/filling processes for biologics requires the containment and transport of compounds within formulation and fill/finish processes. Advancements in film technologies, stirring mechanisms, bioreactor designs, and sensor systems have contributed to the increasing adoption of disposable reactors from the laboratory to commercial use, which further propels the growth of the market.	Low	Investment in R&D, manufacturing equipment and operations to enable production of SUBMCs with the following capabilities: 1) To manufacture SUBMCs to cope with capacity of antibody titers in excess of 10g/L with proprietary expression systems. 2) For expression reaching 10g/L, 2,000L SUBMC must have the capacity to produce 20kg of bulk antibody. This is sufficient for most antibodies, at least during clinical testing. 3) Provider of installation services. SUBMC installation requires not only significant structural support to holds the side walls of the bioreactor, but also needs to provide some temperature control, and support for instruments and sampling ports.	High	• Gaining marketing approval • Acquiring validation of compliance • Global logistics and distribution networks

	Ready-to-Fill & Port Bag Containers	Ultraclean RTF tubs and high barrier port bags remain an integral part of the syringe, vial and cartridge assembly value chain and drive high EBITDA (Earnings Before Interest, Taxes, Depreciation & Amortization) margins (20-35%) at both pre-assembly and fill/finish stages, however, there is a limited customer set which may relegate the opportunity.	High	To cope with contract manufacturer requirements, client needs to implement a flexible manufacturing infrastructure with the latest technologies and with high turnover objectives to strengthen its core competitive advantage of being able to deliver customised RTF tubs and high barrier port bags in a JIT manner. For contingency planning, the client has already successfully used *Isotech*® and *SealScience*® in its Medical Device portfolio. There are opportunities for these to be adapted and exploited in Fill & Port Bag Containers applications.	High	• Biocompatibility • Gaining marketing approval • Acquiring validation of compliance

	HVD Product	Strategic Rationale	Transfer Capabilities	Client Change Requirements	Profitability	Stop Gaps
In Process Transport Products	Clean Rapid Transport Ports (CRTPs)	Low competition from the single supplier CRL as a recent market entry product (2014), albeit with low relative EBTIDA margins (10-15%) due to mainstream DPTE customer use. Opportunities for propriety ownership unlike the DPTE® brand. Uses minimal handle rotation to break the seal on the beta container, reducing operator effort for safer handling alternative to DPTE Alpha ports.	Medium	Design and manufacturing specifications of CRTP must meet RTP chamber test parameters for airflow velocity, particle counts, pressure decay of leakage, and sterility.	Low	• Low ROI. • Gaining marketing approval. • Validation of contamination control.
	Closure Processing Systems (CPS)	Capital intensive to meet FDA's Aseptic Processing guidance yet with strong margin potential (20-40%). Most current suppliers focus CPS development around isolator design or Restricted Access Barrier Systems (RABS). Product development rationale would need to be underpinned by materials science knowhow, closed system design, and automation technology to win this segment	Low	High working capital needed to design and manufacture a viable market contender. Components of CPS should be compatible with the manufacturing equipment for viable commercialization of the product. Compatibility with other component systems is a major consideration in selecting CPS components.	High	• Stringent physico-chemical and biological testing required to meet sterility and safety standards. • Gaining marketing approval.

				Blowback designs of vials and stoppers have to be considered to ensure effective seal-ability of selected vial and stopper combination.		

	HVD Product	Strategic Rationale	Transfer Capabilities	Client Change Requirements	Profitability	Stop Gaps
In Process Transport Products (continued)	DPTE Beta Containers	Large market share from Getinge AB translates to low to medium margin potential (10-20%). There has been little else introduced for this product segment since Getinge AB introduced a patented DPTE® sterile transfer system (October 2018), including the Beta container. Currently available in PE or stainless steel containers, Tyvek™, PU or PE bags - for multiple connections. Therefore considerable material science investment needed to overcome staunch competition and to offer product differentiation.	Low	To compete with the robust technology of Getinge AB, R&D investment needed to address challenges associated with DPTE Beta connectivity; 1) Most systems require the Beta part to be rotated for connection. This can be cumbersome in the case of Beta parts that are heavy and/or bulky and when the rotation requires substantial torque. 2) Design and technology improvements needed to overcome manual control required to connect the Alpha and Beta parts during operation mainly due to its shape. This is more problematic in a real-life situation when this operation has to be done via a manipulation system (glove or glove port) at a high turnover.	Medium	• Design of the container to cope with high productivity targets, production throughput and hence in transfer operations • Stringent security (interlocking between isolators/RABS) requirements, both for the transfer port user and for the transfer itself • Greater emphasis on ergonomics, driven by the evolution of labour legislation around the world to protect operators from musculoskeletal disorders.

	HVD Product	Strategic Rationale	Transfer Capabilities	Client Change Requirements	Profitability	Stop Gaps
In Process Transport Products (continued)	Glove Leak & Transfer Leak Testers (GLTs & TLTs)	GLT & TLT market is projected by the end of 2024 to command $1.8 billion with a CAGR of 6.4% during this period. Although this market segment is saturated with several key players: Franz Ziel, Bosch Packaging Technology, Comecer, Tuv Sud Psb Pte., Mk, Extract Technology and Getinge AB, there is broad product differentiation in terms of wireless, multiple port and Transfer Leak Tester (TLT) features. A high demand market segment as gloves constitute the most vulnerable link in the containment barrier and must be tested for leakage prior to each production batch (Annex 1, EU cGMP guidelines).	Low	R&D and technology inputs to introduce a pressure decay detecting device that improves on the current market status of: 1) Reliability and repeatability down to a 100µm hole diameter. 2) Short testing timelines of ≤20 minutes, short enough for everyday testing. 3) Ergonomics and technology allow for easy handling.	High	• Stricter preventative maintenance programs and new glove or sleeve (gauntlet) assembly technology Introduced impacting on lower leak incidences. • The choice of durable glove materials, coupled with a well-justified replacement frequency, are key aspects of good manufacturing practice and thus in principle minimises the need for GLTs & TLTs, albeit it is a regulatory requirement for testing of leakage prior to each production batch

	HVD Product	Strategic Rationale	Transfer Capabilities	Client Change Requirements	Profitability	Stop Gaps
In Process Transport Products (continued)	Isolators	Stricter sterility controls on *Drug A* manufacturing, translates to a medium margin potential (20-30%). At the high value end of the in-process/transport segment, isolators in contrast to RABS mitigate the most significant risk of manufacturing *Drug A*, human intervention. Although capital intensive and installation time-intensive, it fits with our high value differentiated portfolio objective. Unlike its patented DPTE® sterile transfer system, Getinge AB holds no registered proprietary rights over the Isoflex-R and S designs.	Low	R&D and technology inputs to make the following improvements on the current market status of: 1) Difficulty in transferring materials in and out of the unit. Routinely, it is necessary to connect a smaller docking isolator, which itself is further sanitized using vaporised hydrogen peroxide (VHP) in isolation before moving materials across. This process can be cumbersome, restrictive, and lacks the flexibility for the operator or engineer to rapidly intervene in the event of unexpected issues. 2) The qualification of VHP systems in isolators can also be challenging. For example, VHP is a surface sanitant, meaning when a unit is gassed with the substance, it only hits the exposed surfaces. As an item is moved, it may expose further surfaces that have not been exposed to the sanitizing gas. As a result, there is a need to suspend significant portions of the load within the cabinet to minimize the obscured surfaces. 3) In addition, residual VHP within isolator cabinets has the potential to negatively interact with the drug product itself.	Medium	• Manufacturers switching to RABS due to affordability and flexibility. • Currently there is no legal requirement that isolators should replace RABS. However for RABS it is clear that their use in place of more cumbersome VHP isolators can deliver significant time savings to certain parts of the PDMS space, speeding up the manufacturing process and offering the flexibility.

	HVD Product	Strategic Rationale	Transfer Capabilities	Client Change Requirements	Profitability	Stop Gaps
Finished Products	Aseptic Prefilled Syringes	PFS finished packaging can offer high volumes, albeit with lower relative EBTIDA margins (10-20%) as the packaging does not require the same barrier requirements post-fill and finish.	High	R&D and technology inputs to make the following improvements on the current market status of: 1) Achieving the correct individual conjunction and interaction of the syringe parts in order to enable both functionality and usability. When administering the *Drug A* with the syringe, the plunger rod must operate in concert with the other components, especially the glass barrel. To achieve this, a lubricant coating is placed on the inner surface of the glass barrel. Therefore, a key challenge is to define the appropriate coating process and to control the correct amount of lubricant needed to enable the best possible movement of the	Low	• Numerous key providers in this segment – Gerresheimer, Nemera, Noble, Schott Pharma, Vetter and West Pharma, to name just a few. • Some *Drug A* require small filling volumes and this creates an increased demand on all production areas, including process design, technical equipment, and packaging material.

				plunger rod. This must be achieved in a manner that avoids any form of interaction between the lubricant and the drug substance. 2) *Drug A* biologics react with far greater sensitivity to environmental influences such as heat or light than other substances do. Thus it is important to design, develop, and implement the correct product-related production processes. Hence biocompatibility is vital. 3) Implementation of a suitable dosing method and proper pumps in the filling process is critical. 4) Patient centricity of use and design needs to be factored in; a key discussion point in the upcoming Prefilled Syringes and Injections Summit Meeting, September 2019.		

	Transdermal Patches & On-Body Devices & Implantables	Micro-needle, transdermal & intradermal drug delivery systems represent flexible packaging segments with high margin potential (25-40%), given the greater need for light, oxygen and moisture barriers, complex laminates necessary due to proximity to drug compounds. Potential for desiccant-coated materials to extend shelf life for therapy applications that are especially sensitive.	Low	R&D and technology inputs to make the following improvements on the current market status of: 1) Wearable on-body drug delivery devices capable of delivering high volumes and viscosities with minimal discomfort. 2) Construction materials, injections process, and safety features, to overcome the challenges of delivering large-molecule and high-volume biologics. 3) The proprietary sequential elastomeric toroid mechanical drive system that enables the force required to deliver the drug, but not to alter the administration volume, using the smallest possible needle size, typically 31g.	High	• As this is a self-administration device, anticipated regulatory approval timeline would be long and of high cost. • Patient training and education requirement is an additional logistical and cost hurdle.

Critical Success Factors to be a Market Winner:

- **Flexible packaging and development** – the PDMS space is comprised of a broad category of segmented markets, made up of an array of packaging options, for example plastic, glass, small and large volume bags, ampoules, vials, prefilled syringes, ready-to-fill syringes and cartridges, as well as ready-to-mix systems. As packaging has become more flexible, so has the machinery needed for its production.i3 Consult can conduct an internal audit of the present operations within the client's production infrastructure to propose what systems would be needed to attain the machine flexibility to meet future PDMS needs. Flexible machine platforms offer the PDMS provider the ability to make more kinds of packaging products. As for preliminary planning on this critical success factor need, the client would be advised to consider the decision trees Figures 2 and 3[3] for understanding the requirements of sterile packaging for aqueous product and non-aqueous liquid, semi-solid or dry powder product sterilisation respectively. In particular for assembly and in-process/transport stages of the *Drug A* manufacturing, the packaging specifications must meet the requirement of the product handling scenarios. For example aqueous product packaging specifications of sterilised aqueous products would need to meet scenario outcomes of auto-claving at 121^{o}C for 15 minutes, moist heat sterilisation ≥8minutes and maintaining a SAL of ≤10^{-6}, use of pre-sterilised individual components and aseptic compounding and filling as well as aseptic filtration and processing combinations. Whereas for non-aqueous liquid, semi-solid or dry powder product packaging specifications of such products would need to meet scenario outcomes of dry heat at 160^{o}C for 120 minutes, maintaining a SAL of ≤10^{-6}, ionising radiation with an absorbed minimum dose of ≥25KGy, handling formulations filtered through a microbial retentive filter, use of pre-sterilised individual components and aseptic compounding and filling as well as use of filtration and aseptic processing. Therefore for planning of flexible machine platforms, the client needs to consider design and technology capabilities that will enable them to manufacture the packaging materials to meet these possible product scenarios during the assembly and in-process/transport stages.

[3] Source: EMA/CHMP/CVMP/QWP/BWP/850374/2015

Figure 2: Decision tree for aqueous product sterilisation

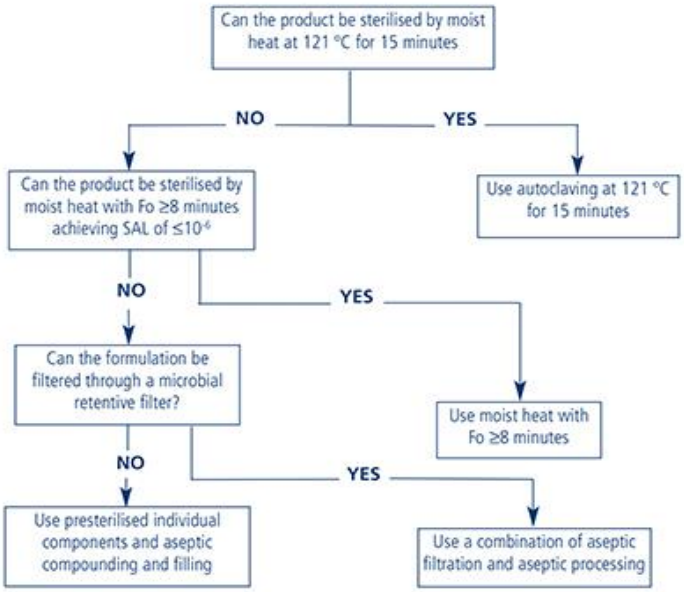
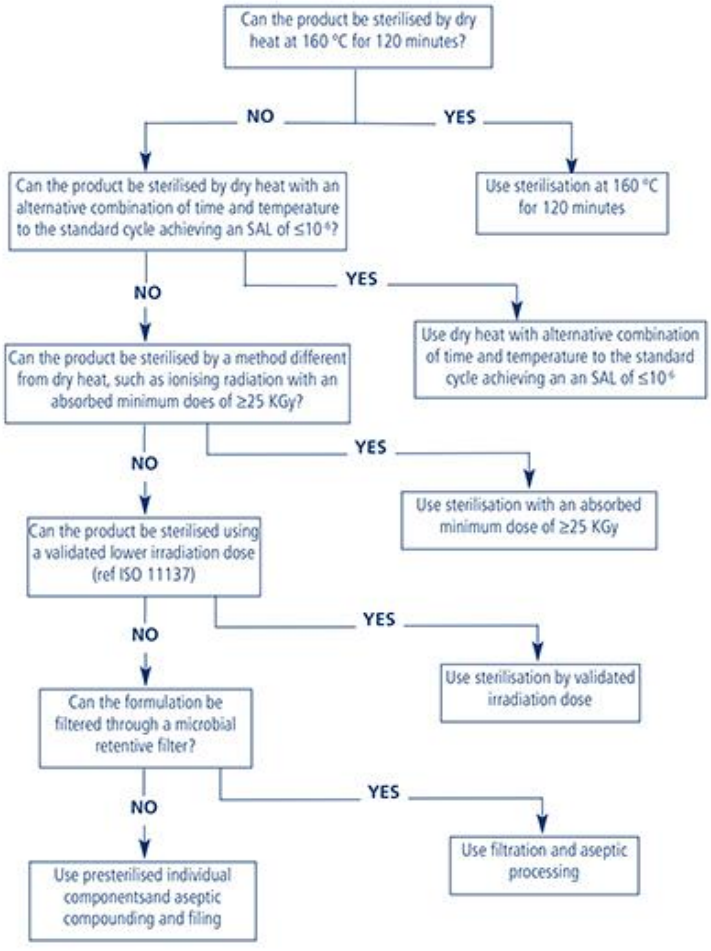


Figure 3: Decision tree for non-aqueous liquid, semi-solid or dry powder product sterilisation



- **The challenge of an automation solution** - The FDA has recommended automation in pharmaceutical manufacturing, although for biopharmaceuticals, the technology is still in its early stages. Continuous manufacturing of PDMS packaging materials is attractive because it offers both time and cost benefits. Automated production lines are able to run 24/7 while reducing labour costs and therefore create a higher profit margin or opportunities for competitive pricing for the client. Although automation technology is easier to achieve in oral solid dose and small-molecule API packaging production, the client would increase its long-term competitiveness by investing in R&D in the quest for continuous solutions in the manufacture of next-generation *Drug A* packaging.

- **Implementing single use technology** – This technology is used in *Drug A* manufacturing of antibodies, proteins, vaccines, cell therapy, and gene therapy. Despite being the current manufacturing solution, a single-use strategy comes with its own unique set of challenges. The uneasiness associated with single-use technologies includes the compatibility of parts among different suppliers. As quoted by the global head of next generation system development, life science, upstream and systems business, *Company Z*, *Steve M*:

"Implementing single-use brings with it new challenges that traditional facilities do not face, such as ensuring skids from different vendors have compatible connectors and common spare components such as clamps."

Another challenge lies in the in-process transport stage of scale-down or scale-up, depending on the size of a reactor. Consider a typical reactor is 50 L and commercial scale is 2000 L, scale-up or scale-down may not be operationally feasible or come with too high a cost.[4] Therefore opportunities exist for the client to provide a complete upstream to downstream SUS packaging solution to ensure compatibility of packaging parts in all product segments - assembly, in-process and finished products. This SUS packaging solution should also address the challenge of scale-up and scale-down in the in-process transport stage. For further analysis on this critical success factor, see the *Deliverable 4: Market Assessment of Competitors Providing Product and Services to SUT/SUS Manufacturers*.

- **Implementing Quality by Design (QbD)** – *Drug A* manufacturers are adopting QbD into their processes in order to eliminate any risk of contamination. Particulate contaminants in *Drug A* products have contributed to drug shortages, which is the worst-case scenario that no company wants to bear. Therefore part of the PDMS capabilities in providing solutions to client manufacturers, is to incorporate QbD elements into their packaging products ensuring that they are compatible throughout all processes of *Drug A* production. There is a certain pain point in providing packaging process solutions for pre-filled syringes - it is not uncommon for proteins to interact with the components of the packaging systems under certain conditions. The client is advised to adopt QbD approaches in their product development so as to prevent such a scenario. With each QbD element introduced, the client should be optimizing all internal quality management systems through audits, visual inspection, and the design of systems for product monitoring that will alert manufacturers to any potential risk of a hazard occurring.

[4] http://www.pharmtech.com/parenterals-particulates-and-quality-design Accessed July 2019

The purpose of QbD is to manufacture correctly from the start. Time and cost are the pain points to ensuring a facility's QbD. A QbD approach to quality requires increased testing and labor in research and is often the outcome of a strategic partnership with suppliers and this poses a key market opportunity for the client. Just as the client has strong capabilities in providing technical services such as process validation and packaging testing for the medical device arena, through selective hiring, comprehensive training and well-funded research, it is highly feasible for the client to offer similar services for QbD troubleshooting in the PDMS space.

- **Developing patient-centric packaging solutions** – Partnerships are common in the pharmaceutical industry. So it should come at no surprise to the client that *Drug A* programs and its packaging can work together to improve patient compliance and treatment efficacy. Current estimates are that prescription non-adherence costs the US healthcare system roughly $330 billion annually.[3] Products that combine a drug or biological API with a device, such as drug-eluting stents and drug delivery systems, can offer valuable approaches for treating today's challenging chronic diseases. The number of product categories and individual product offerings in the drug-device combination market has grown to be enormous. According to BCC Research, sales of drug-device combination products are expected to reach $31 billion by Q4 2019. [4] The biotech industry has an invested interest in drug-device combination products such as auto injectors, pen injectors and wearable injection devices, because these drugs tend to be highly viscous and require high dosing. While some companies have device and packaging capabilities internally, others outsource to companies to small to mid-size companies with high tech medical device development capabilities. As medical devices become more sophisticated and sensitive, using packaging that protects the high-value device and still appeals to consumers is critical. Adding digital printing also allows the data on every individual unit to be read and exploited in order to ensure that the patient is taking the right drug and receiving the right dose, at the right time. As proper drug delivery becomes increasingly critical going forward, pharmaceutical and biopharma packaging must remain patient-centric by being safer, simpler and smarter.

Deliverable 4: Market Assessment of Competitors Providing Product and Services to SUS Manufacturers.

Whilst in Deliverable 2, the Five Force Framework gave insight into the competitive dynamics of the PDMS space, the client needs to understand how their organization is positioned relative to the other competitors *within* the PDMS industry.

Even within the PDMS space, not all competitors will be following similar strategies or competing directly against each other. As alluded to in Deliverable 3, developing product and services to meet the challenging needs of SUS drug manufacturers, is one of the most important ways of winning in the PDMS market. We suggest here the use of *strategic group analysis* to identify the ways in which particular groups of companies compete to provide product and services to SUS drug manufacturers. The key to this approach is to identify three or four sets of characteristics that seem to establish key differences between the companies competing to provide product and services to SUS drug manufacturers. In Table 6, the strategic group is aligned with the competitor(s) who adopt this strategy as a SUS solution and the rationale for adoption.

Table 6: Alignment of Strategic Groups with Competitor(s)

Competitor(s)	Strategic Group	Rationale
Company Y & *Company Z*	SUS packaging caters for buffer solutions and cell-culture media production	• Time reduction to perform cleaning and cleaning validation. • Enables multi-molecules to run in the same facility. • Quick turn over from one product to another, or from one batch to another batch. • Enables connection of two unit operations, thereby minimizing hold time and enabling continuous processing. • Reduce overall operating costs by minimizing or eliminating the need for clean in place (CIP)/sterilize in place (SIP), reducing analytical quality control costs specifically for raw materials such as buffer solutions and cell cultures and therefore improving facility utilization time.
Company S & *Company W*	SUS packaging for end to end scalability	• Production scales in the PDMS space are between 15 L to 2000 L. To cater for 1000 kgs per annum of product or less and manufactured in single-use bioreactors up to 2000-L scale or less. • Representative scale-down models of single-use bioreactors are typically at 50L scale, in the current market are expensive and also not convenient to use. • To be able to accommodate traditional fed-batch cell culture processes as well as perfusion processes. • To offer increased flexibility to adapt to a wide variety of different processes at different scales coming through the pipeline.
Company Z & *Company W*	SUS packaging compatibility between single-use systems	• Eliminating significant differences in the design details so that it doesn't pose challenges when it comes to system compatibility between products from different suppliers. For example, agitation/mixing and gas sparging designs need to be made compatible, as currently they are quite different among the single-use bioreactors from the several major suppliers. • Circumvents the end-users need to carefully understand and evaluate the design features of the various products. • Process transfer using the actual production cell line is made easier. • Potential product quality impacts are minimised. • Makes operator life less complex and minimises opportunities for errors.

Company S	Packaging accommodates for hybrid process design	• Connectivity between SUS and stainless (hybrid process design), with a sterile connector, for example the Opta from *Company S*. The Opta is autoclavable and connects to a stainless-steel vessel and then autoclaved together with the vessel. This vessel can then be connected to a SUS equipped with an Opta counterpart. • This fulfils two requirements as cited above – scalability and compatibility.
Company S & *Company Y*	SUS packaging demonstrates end to end biocompatibility	• Recent industry reports[5] show that biocompatibility testing did not always detect cell growth issues. The report also cited cytotoxic leachates and this has led to the need for new evaluation techniques and testing to determine potential impacts of plastics used in SUS on cell culture plastics. • Testing system to ensure that different buffer solutions or cell-culture media has no impact on the integrity of the single-use component bags for example. • Ensure SUS packaging is 100% impermeable to air. Thus buffer pH, conductivity, or stability of solutions is not compromised.
Company S	Acquired validation status as an SUS packaging supplier	• Supplier quality and manufacturing systems must be cGMP compliant. • Ensure that the level of compliance is consistent across supplier sites. • Manufacturing environment ensures SUS components are manufactured to ISO class 8 or better. • Have in place customer change notification and complaint management processes.

[5] S. Haigney, "Integrating Single-Use Systems in Pharma Manufacturing," Pharmaceutical Technology 40 (6) 2016.

Companies are also unlikely to compete for the same customers. The preferences and needs of SUS manufacturers differ, so not all products and services are likely to meet their requirements. By identifying these different requirements through *market segmentation analysis*, it can be proposed to the client how they can adopt strategies to more closely appeal to the needs of particular groups of SUS manufacturers, so defining a position within the market that is more favorable relative to the forces of competition. The market segmentation analysis aspect can be conducted and reported at the discretion of the client.

Deliverable 5: Feasibility case studies of ultraclean, rapid prototyping, material & design expertise and trouble-shooting services. Define what Company X needs to offer to win in these PDMS segments.

For each one of these service offerings - ultraclean, rapid prototyping, material & design expertise and trouble-shooting, a step wise approach has been performed treating each as a strategic business unit (SBU) and using research findings from key market leaders in the PDMS space who offer such a service.

Step 1: Determined whether there are any insurmountable obstacles in terms of capital requirements for entry or continuing operations are unavailable or unaffordable. A "yes" response indicates that the product/service offerings have little chance for success.

Step 2: Feasible projected income over the next five years.

Step 3: Feasible to acquire >5% market share against total volume in the market area

Step 4: Assessed operational feasibility. Technical feasibility and costs involved in start-up, fixed investment, and operation were considered

Step 5: Estimated the asset requirement based on an opening day balance sheet. Necessary assets included everything from cash necessary for working capital to buildings and land.

Step 6: If there were no areas of concern in the above steps, then this indicates a high feasibility rating (shaded in green), one of two areas of concern (highlighted in **bold**) borne out of these steps rates as medium feasibility (shaded in amber), three or four concern areas equates to low feasibility (shaded in red) and therefore any score greater would be classified as a “no-go” product/service segment. These findings are presented in Table 7.

Upon access being granted to the client’s financial statements, these findings should be analysed for further refinement and recommendations put forward.

Table 7: Feasibility Case Studies of Ultraclean, Rapid Prototyping, Material & Design Expertise and Trouble-Shooting Services in the PDMS Space

Product/Service	Step 1	Step 2	Step 3	Step 4	Step 5	Step 6
Ultraclean	No	Feasible	Feasible	Feasible	**$1,500 Million**	Medium
Rapid Prototyping	No	Feasible	Feasible	Feasible	**$1,300 Million**	Medium
Material & Design Expertise	No	Feasible	Feasible	Feasible	$300 – 700 Million	High
Trouble-Shooting Services	No	Feasible	Feasible	**Not Feasible**	$200 - 500 Million	Medium

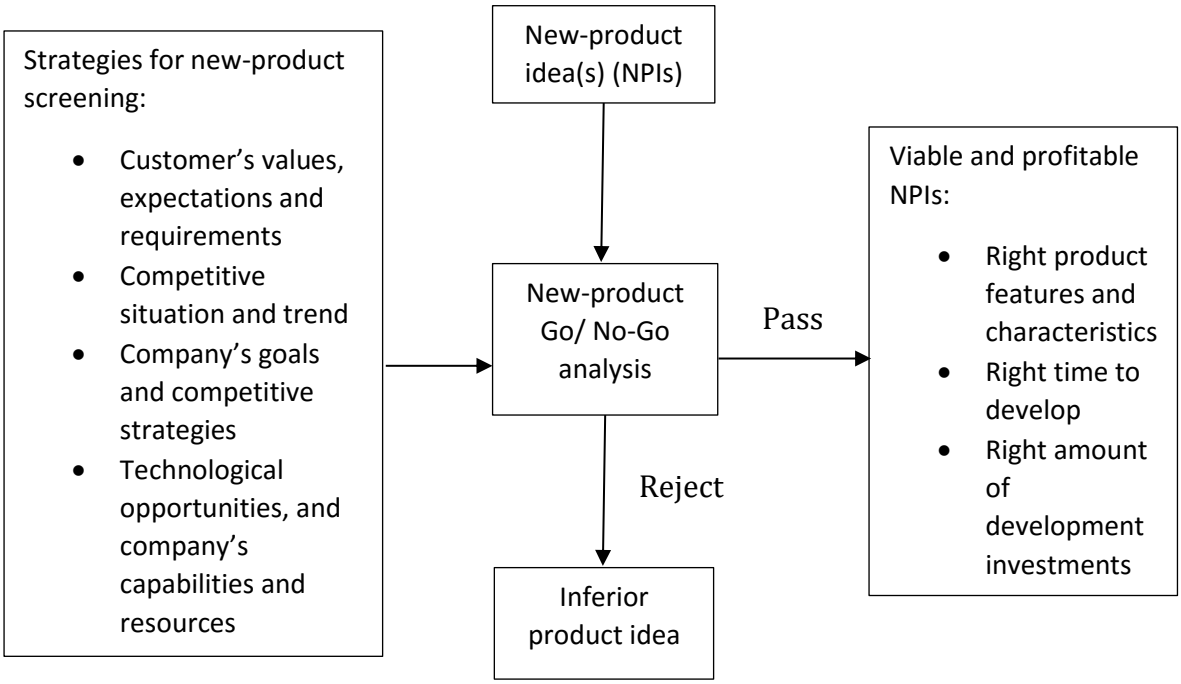
Deliverable 6: Go/No-Go analysis on development of Clean Rapid Transport Ports (CRTPs), Closure Processing Systems (CPS), DPTE beta containers, Glove Leak Testers & Transfer Leak Testers (GLTs & TLTs) and Isolators.

The PDMS competition entails that the screening of a new product concept is perhaps the most critical activity in new product development (NPD). Both the unknown nature and the timing of NPD in this new product screening (NPS) may limit the client, as it is associated with uncertainty and complexity.

Even with an improved NPD process, competition and emerging new technologies can still limit the NPD success rate to no more than 59%, and it still requires 6.6 ideas to generate a successful product[6], the same level as 20 years ago! Here as a holistic approach to Go/No-Go analysis on the HVD product offers in the PDMS space, the scheme shown in Figure 4 when applied to the current market offer is intended to give the client a realistic Go/No-Go decision on each of these HVD product offers. Similar to Deliverable 5, if there are no areas of concern in applying this Go/No-Go analysis, then this indicates a "Go" recommendation (shaded in green). For any areas of concern (highlighted in **bold**) equates to a "No-Go" recommendation (shaded in red). The results of the Go/No-Go analysis are shown in Table 8.

Upon access being granted to the client's financial statements and financial planning reports, these findings should be analysed for further refinement and recommendations put forward.

Figure 4: A Holistic Approach to Go/No-Go Analysis



6 A. Griffin, "PDMA research on new product development practices: Updating trends and benchmarking best practices," J. Prod. Innov. Manage., vol. 14, pp. 429–458, 1997

Table 8: Outcomes of Go/No-Go Analysis on Current HVD Product Offers in the PDMS Space

HVD Product	Strategies for NPS	Viable & Profitable New Product Idea(s)	Go/No-Go Recommendation
CRTPs	Fits with company's mission "to safely deliver life-saving products" and qualifies as a HVD segment. Technological opportunities exist, but **company's current capabilities and resources are not met**.	**Already a mature market and therefore would require a large investment to engineer and develop a new prototype to reach a "market winner" position. Projected profitability of the market is low.**	No-Go
CPS	Customer requirements are compatibility with both RABS and Isolator processing. A good fit with company's strategy to win a HVD segment. Technological opportunities certainly exist, and company has capabilities and resources in terms of design and development, refinement and validation processes for a market launch	With further research and design initiatives, suitable product features and characteristics can be found especially to meet the CPS compatibility challenge and market is ripe for this to be the right time to develop. **Concern at this point is, does the company have sufficient cash flow to afford development investment required?**	No-Go
DPTE beta containers	Customer's expectations and requirements is that there could be improvements in the product design to cope with operator handling challenges. Hence there is a competitive situation to invent a new prototype. Company has capabilities and resources in terms of design and development, material research and procurement, refinement and validation processes for a market launch.	With sufficient R&D inputs, all criteria of product features, characteristics and time to develop can be met. **Current concern is if the right amount of development investment is available.**	No-Go

GLTs & TLTs	Customer's expectations and requirements are that these should be user friendly and not disturb batch processing. Only two or three main competitive players with a strong trend for more entrants as this is a highly differentiated segment. Fits with company's strategy to win HVD segments. **There is a large technology input requirement for development and the company would need to outsource to specialist technology providers to meet this gap**.	If the technology input gap can be filled criteria of product features, characteristics, timing as well as investment requirements can be met.	No-Go
Isolators	A good proportion of the manufacturer customer's expectations is that this is the only approach to sterility handling of *Drug A*. There is a strong competitive situation and with a positive market trend. It represents a very good fit with company's strategy to win a HVD segment. **However the company's capabilities and resources are not synchronised with the technological opportunities.**	It is the optimum time to develop product features and characteristics. **Uncertain if sufficient amount of development investments can be met.**	No-Go

Deliverable 7: Retro Analysis Reporting (from the lowest downstream point, e.g. Drug A administration to the patient to the highest upstream point of the process, e.g. bioreactor mixing) identifying blind spots, stopgaps and value chain improvements focusing on a reduced product development timeline, reduction in costs of labour, material and utilities, increased process efficiency, increased productivity, and reduced risk of cross-contamination.

It is not just the clinical development of the API which can fail regulatory authority approval but also the packaging of the drug candidate. In the *Drug A* development this is more critical than perhaps other drug formulations. Hence it is important to retrospectively analyse and trace "backwards" all the stages of the *Drug A* packaging process from the lowest downstream point, e.g. *Drug A* administration to the patient to the highest upstream point of the process, e.g. bioreactor mixing making sure the client does not "fall between the stools" in the PDMS space. In fact being the packaging supplier to a Pharma or CDMO at the downstream point is more likely to be for the delivery of the *Drug A* candidate at the late clinical phases II/III or approval stages than that for the higher upstream points whereby preclinical studies are still being conducted and the *Drug A* administration method for the animal subject needs adapting or may still be under development. Hence the lower downstream packaging segments represent greater long term opportunities albeit finished product packaging represents a lower value segment, thus on a unit price per sales basis, revenue volumes tend to be smaller. On the premise of pursuing a one stop shop packaging supplier strategy from upstream to downstream for Pharma or CDMO customers, this retro-audit trail places importance on value chain improvements *at all stages* of upstream to downstream as it opens up opportunities for focusing on a reduced product development timeline, reduction in costs of labour, material and utilities, increased process efficiency, increased productivity, and reduced risk of cross-contamination all of which can be revealed in this analysis. Table 9 highlights the key blind spots, stopgaps and value chain improvements at each stage of the *Drug A* packaging process.

Table 9: Key Blind Spots Stopgaps and Value Chain Improvements for the Client in the PDMS Space

Packaging Stage	Blind Spots	Stop Gaps	Value Chain Improvements
Finished Product	Counterfeiting is a major problem in all pharma markets globally particularly in emerging markets such as China where the client has a manufacturing plant in Suzhou	Lack of authentication and serialization features in packaging production systems	Offer a comprehensive serialization solution across all packaging product offers. Client to review its packaging product mix and assign Innovative Packaging Technologies SBU to develop and enable a multitude of combinations — ampoule shape and size, type of glass as well as colour, shape and number of identification rings, including luminescent nanoparticles to offer full counterfeiting protection in the packaging for manufacturers.
	Finished product packaging can be easily tampered with or opened by a teenage child	Perception that all proofing-packaging is sufficient. Designing packaging that meets need for child-resistant (CR) packaging but clashes with the senior-friendly packaging need or vice versa.	Innovative Packaging Technologies SBU to use the latest technology and QbD elements, in creating a package that children cannot open but older adults can. Services to CDMO & Pharma SBU to hold regular and on-going meetings with the Innovative Packaging Technologies SBU. This will enable communication on the needs to be met and exceeded for customers' expectations in providing user-friendly CR packaging solutions while ensuring the fit, form and function of the package is consistent with CDMO/Pharma manufacturer's brand equity and overall value proposition, while keeping within budgetary constraints.

Packaging Stage	Blind Spots	Stop Gaps	Value Chain Improvements
Finished Product (continued)	Finished product packaging marketing myopia	Lack of communication between packaging supplier and Pharma/CDMO customer	Material scientists from client's Innovative Packaging Technologies SBU to partner with pharmaceutical companies to understand the interaction between the drug and the package and based on a corrective communication feedback loop, Innovative Packaging Technologies SBU to come up with customised designs.
	Lack of patient compliance owing to packaging design features or drug administration deficiencies owing to the packaging design	Current drug-device combination product line such as auto-injectors, pen injectors and wearable injection devices, does not meet the patient's clinical and care needs because *Drug A* of large biologic form tend to be highly viscous and require high dosing	Innovative Packaging Technologies SBU to partner with external Pharma/CDMO key opinion leaders in each therapy space, to define what packaging specifications can deliver the *Drug A* at high viscosity and high volumes. Innovative Packaging Technologies SBU to outsource to a technology provider to integrate digital printing into the client's packaging product mix. This digital printing feature should enable the data on every individual unit to be read and exploited in order to ensure that the patient is taking the right drug and receiving the right dose, at the right time.

Packaging Stage	Blind Spots	Stop Gaps	Value Chain Improvements
In-Process	Human operation at the in-process stage has the inherent risk of bio-contamination, musculoskeletal injury and operational error.	Under investment and development of automation technology	Innovative Packaging Technologies SBU to develop an in-house technology for the production of in-process product lines such as Closure Processing Systems (CPS) and DPTE Beta containers that have been designed to minimize human interactions with drug products. Such products should incorporate artificial vision and sterility sensor systems to enable the automatic exclusion of bio-contaminants and automatic inspection of particulates during all the in-process stages. Also automation technology should be introduced to avoid the potential for human error and musculoskeletal injury (especially during manipulation and handling of larger scale batches) in this important unit operation. Automation systems also help reduce the chance for incorrect container manipulation and minimise cross contamination.

Packaging Stage	Blind Spots	Stop Gaps	Value Chain Improvements
In-Process (continued)	In-Process packaging product marketing myopia.	Lack of flexible and scalable in-process packaging solutions.	In-Process packaging plays a critical role in maintaining the quality of a drug product and preventing bio-contamination and impurities. To minimize interaction with the *Drug A*, it is essential that the packaging components' design and formulation meet the containment requirements mandated by the physical and chemical attributes of the drug. Different *Drug A* products have different in-process packaging needs, and what is safe, sterile and effective for one product might not necessarily be the best choice for another. Selecting the right in-process packaging solution for a particular drug product is crucial to ensuring that the drug reaches the finished product stage and with the intended therapeutic effect. To ensure the perfect match between a *Drug A* and its packaging, it is important for the Services to CDMO & Pharma SBU to work closely with pharmaceutical manufacturers from the early stages of drug development through to production and to feedback critical and specific customer needs information to the Innovative Packaging Technologies SBU for product development planning. Establishing a reliable and trustworthy partnership allows pharmaceutical companies to focus on their core competencies: bringing valuable *Drug A* products to the marketplace. This in turn will drive stable long-term revenue streams for the client.

Packaging Stage	Blind Spots	Stop Gaps	Value Chain Improvements
In-Process (continued)	Perceived low importance of QC and validation processes at the In-Process stage	Bio-contamination and/or impurities traced in the In-Process work flow	Services to CDMO & Pharma SBU to be shared SOPs and validation procedures from the pharmaceutical manufacturing customer. This sharing of information will allow the client to monitor the flow of materials from raw materials, in-process and final products and equipment and to quickly trouble shoot so as to provide alternative packaging solutions within the client's product portfolio if there are potential contamination threats. Services to CDMO & Pharma SBU to work closely with pharmaceutical manufacturing managers in monitoring the movement of staff through the facility to ensure all packaging components are in line with cGMP standards in order to minimize contamination.

Packaging Stage	Blind Spots	Stop Gaps	Value Chain Improvements
Assembly	Bioreactor packaging not amenable to hydration and rehydration processes.	Bioreactor specifications and functions do not meet scalability and manipulation needs of large amounts of purified water needed	SUS bioreactors require fully hydrated media in order to take advantage of the benefits of single-use systems. Therefore in the case of dry media, it must be rehydrated with purified water, which requires both the utility, and a disposable media preparation system with cooling. Innovative Packaging Technologies SBU are to develop bioreactors to accommodate these requirements. Purchasing hydrated media at scales of 2,000L and above involves shipping large quantities of water, and large cooled storage spaces (or very well-timed purchasing). Logistics don't always support JIT supply of media, because many media are customised for products, especially feeds. Therefore the client's Packaged Product Outbound Logistics SBU needs to work closely with the pharmaceutical manufacturer managers to resolve this JIT challenge.

Packaging Stage	Blind Spots	Stop Gaps	Value Chain Improvements
Assembly (continued)	Lack of long term storage capability in the assembly packaging.	Over extended time periods, buffers or cell-culture media, in single-use systems can generate extractables and leachables, which may cause impurities.	The client's Innovative Packaging Technologies SBU are to develop an assembly/bioreactor system that enables the biopharmaceutical manufacturer to prepare buffer or media on an as-needed basis by using solid materials that are customized for one single-use tank, rather than concentrated buffer solutions that are already in liquid form. The client is to provide the pharmaceutical manufacturer customer with single-use powder materials in bags or other containers that are pre-weighed and compatible with single-use systems. The packaging that contains the solid can be attached directly to the bioreactor tank and the biopharmaceutical manufacturer can then make the solution, circumventing the long-term extractable/leachable compatibility issue.

Deliverable 8: Potential Disruptor Reporting – Use of the PESTLE framework approach to identify disruptors, 3 and 10 years onwards.

PESTLE (Political, Economic, Social, Technological, Legal and Environmental) represents six macro-business factors and when used as a framework, provides a systematic technique for analyzing the business environment. It enables the client to:

- Summarise the most important influences of the business environment.
- Evaluate the potential impact of these influences on the organization. Using PESTLE analysis can help to highlight the biggest influences on the strategy of the client, both currently and in the future. These influences can be both positive and negative. In addition, influences often cross the divide between the six macro-business factors, the important point is that they appear somewhere in the analysis.

In line with this deliverable, in Table 10, the negative influences or "disruptors" are identified for each of these macro-business factors for projections both in the 3-year short term (2022) and 10-year longer term (2029) in the PDMS space.

Table 10: Projected 3-Year Short Term (2022) and 10-Year Longer Term (2029) Disruptors in the PDMS space.

Macro-Business Factors	2022 Disruptor	2029 Disruptor
Political	A likely no deal Brexit outcome is a potential disruptor to the client's EU manufacturing base in Venray, The Netherlands with delays at custom ports albeit likely at a reduced Euro price for imported materials owing to the weakening of the GB Pound Sterling at the time of writing. In the reverse trading direction, a reduced demand of packaging products and services by UK based pharma manufacturers is likely due to an economic recession impacted by the no-deal Brexit outcome. The scale of the disruption can be anticipated with the current 88 human products under European centrally authorised medicinal product control, sites located in the UK only, manufacture a sizeable 16% of these medicines.	Increasing harmonization pressure from ICH on *Drug A* sterility and packaging requirements. For example tightening of ICHQ3D for elemental impurities.
Economic	Additional tariff of 10% on the remaining $300 billion of goods and products coming from China to be imposed by the Trump administration is likely to be reciprocated by China. Therefore prices of packaging materials imported from/exported to China are likely to rise during the short term until a new trade agreement can be ratified.	Global 'Not For Profit' *Drug A* supply for developing countries
Social	Personalized healthcare for *Drug A* administration (this could be both a positive and negative influence). Raised consumer expectations regarding packaging formats and features.	Health awareness (prevention) programs positively impacting on healthcare outcomes but driving down *Drug A* therapy needs due to lower chronic disease incidence.

		Aging populations put demands on packaging formats to solve the child-protection vs. senior friendly paradox (this could be both a positive and negative influence).
Technological	Pharma manufacturers demanding to process different products and containers on the same machine and simultaneously minimizing changeover times. Fast changeovers between different packaging containers become critical with robotic control the only way to cope with this production design. Large biologic molecules derive highly viscous drug formulations, requiring high-dosage accuracy. This demands higher dosage volumes with longer administration times necessitating device integration for convenient self-administration outside the clinical setting (this could be both a positive and negative influence).	"Theranostics" become more clinical routine than "Therapeutics" (Dx > Rx). Patients will be prescribed or monitored with AI devices to prevent the disease rather than being prescribed the *Drug A* treatment. Novel drug administration technologies as an alternative to the current common *Drug A* routes of intramuscular (IM), subcutaneous (SC) and intravenous (IV) (this could be both a positive and negative influence).
Legal	Volume of bio-generics and bio-similars impact on regulatory authorities to impose stricter cGMP guidelines.	Heavy legislation on industry offenders not complying with sustainability policies. Legal requirement for packaging manufacturers to justify their carbon footprint in all their processes. Genetic discrimination of *Drug A* treatments
Environmental	Pressures from environmental lobbyists to justify the high turnover of raw materials needed in SUS based *Drug A* manufacturing and packaging.	Development and emergence of specialist vertical *Drug A* therapy providers with manufacturing, packaging and treatment portfolios.

Deliverable 9: Identify any key market/product for heightened focus and why.

In consideration of the market analyses and internal audits given in this report and in alignment with the client's strategic objective to penetrate and win in the HVD segments of the PDMS space, it is proposed that the client focus on the following:

- Given that the 3P's – product, process and patient are driving this PDMS market, sizeable investment is needed in research innovation and product development to position itself strongly as a HVD packaging provider for SUS based biopharmaceutical manufacturers e.g. single-use powder materials in bags connectable to bioreactors has unique appeal to the prefilled and ready-to-use container segment.

- Further investment and collaboration with technology providers to launch smart on-body devices and implantables is a key focus as this represents a HVD product with high margin potential driven by the patient friendly demand factor.

- Material science, technology inputs and process design elements to be incorporated into the client's HVD product line to meet upstream to downstream biopharmaceutical manufacturer requirements on packaging flexibility, scalability and assured sterility. Integration of automation using robotics and AI systems into the client's core manufacturing systems is success critical for continuous production of these products.

- Smart raw material options are needed in packaging materials as a unique selling point on biocompatibility, bio-burden, leaching and sterility challenges. To remain competitive in the PDMS space, large R&D investments in order to launch packaging products with newer types of material to manufacture *Drug A* packaging containers is mandatory, as the global market is suddenly a hotbed of opportunities for manufacturers. For example, polymers such as cyclic olefin polymers (COP) and cyclic olefin copolymers (COC) are in huge demand, due to their inherent advantages over conventional plastic and glass used to manufacture *Drug A* packaging containers. The introduction of smart or improved raw material types augments increased sophistication in drug delivery technologies thereby helping biopharmaceutical manufacturers increase their revenue standing in the global market and consequently such revenue margins are ultimately passed onto the client.

- Front line business development efforts, e.g. from the client's Services to CDMO & Pharma SBU (see Deliverable 1) are needed for strategic collaboration between biopharmaceutical manufacturers for both the sourcing of appropriate raw materials and the final packaging formats.

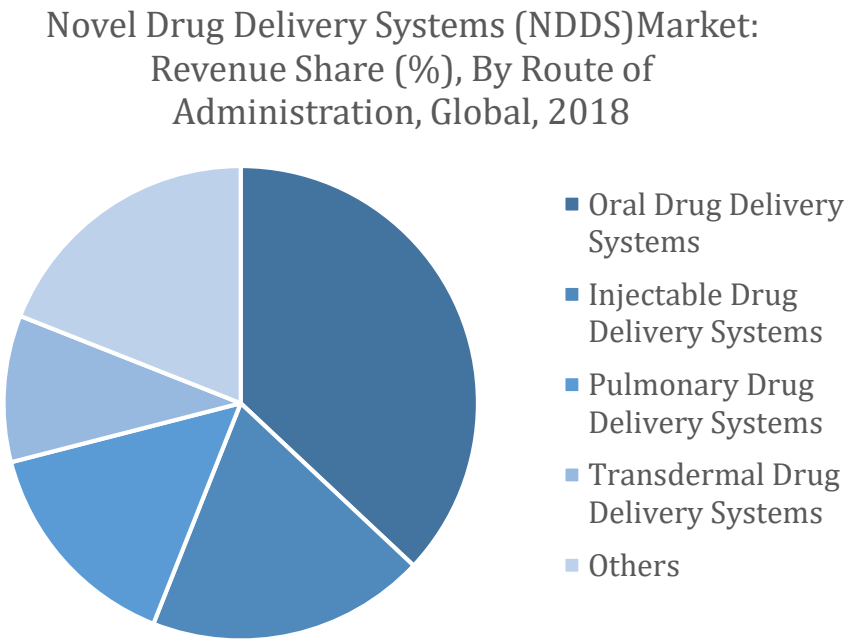
Deliverable 10: High level reporting on Market Size and Share from in-house data available.

According to a report released last month by Future Market Insights[7], the global *Drug A* packaging market is set to exceed $10 billion by the end of 2018. Exhibiting a growth rate of 4.8% in the coming decade, revenue from the sales of *Drug A* packaging products is slated to cross $16 billion by 2028.

Soliciting and acquiring reliable market size and share data is a premium price process with even off shore market research companies commanding prices of $2000 to $4000 for generic data requests.

Our core team of experts and our 200000 plus network has been able to find some "needles amongst the haystack" on the market size and size for both present and future *Drug A* delivery markets. These are set out in the following Charts 1, 2, 3 and 4.

Chart 1: Global share of Injectable Drug Delivery Systems and Transdermal Drug Delivery Systems segments represent collectively 30 to 40% of the total NDDS market revenue share



[7] https://consumerreportsreview.com/parenteral-packaging-market-report-explored-in-latest-research/ Accessed August 2019

Chart 2: Outlines some of the key market indicators for the transdermal drug delivery market. Considering that this is one of the key routes of administration for *Drug A* administration some forecasts and extrapolations can be taken from this data set.

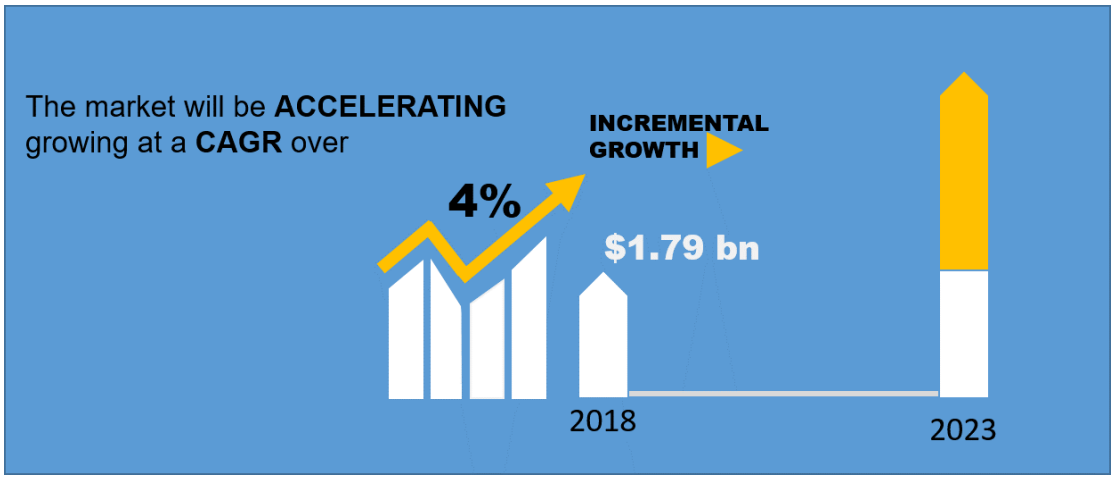


Chart 3: India is a high potential emerging market with a therapeutic injection segment of the large volume *Drug A* market worth $29 million by 2024

India large volume *Drug A* (LVP) market size, by application, 2014-2025 (USD Million)

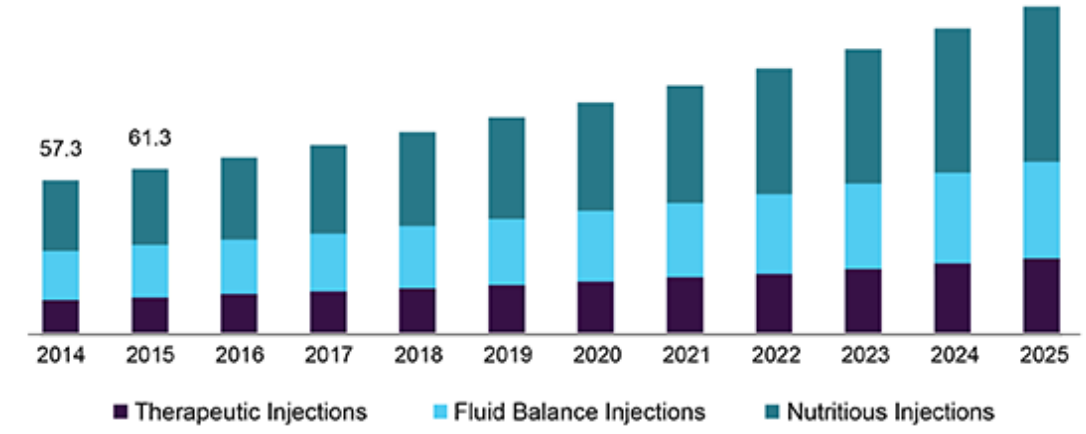
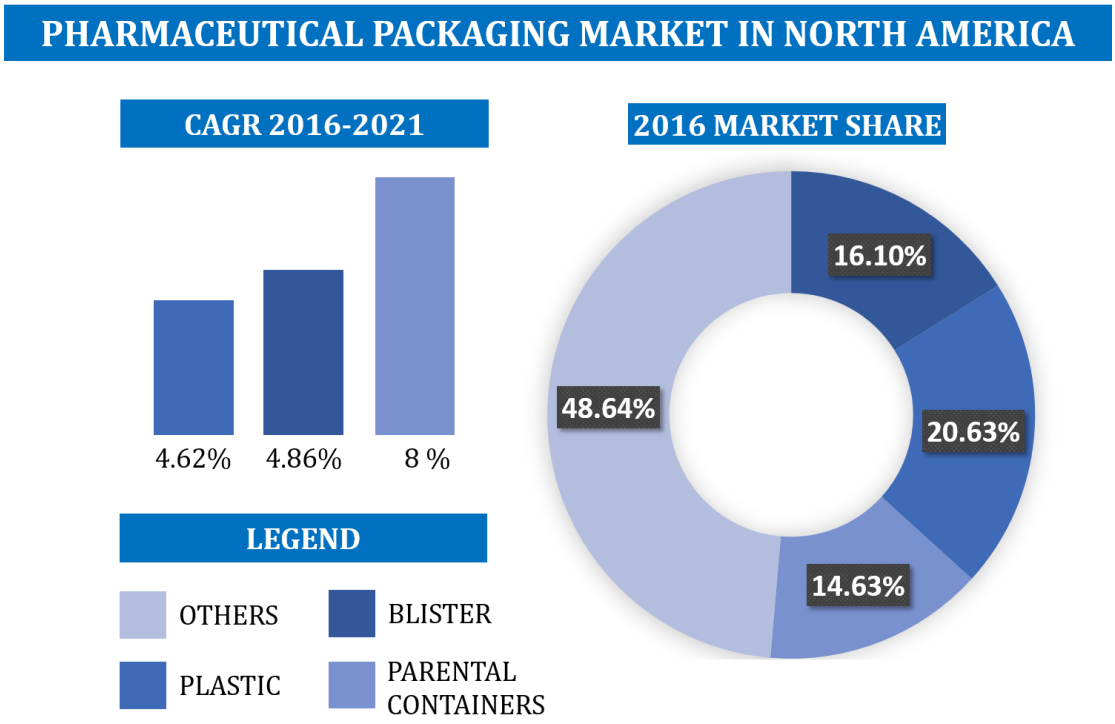


Chart 4: According to a report released by Technavio[8] pharmaceutical *Drug A* containers packaging market in North America will reach a revenue of $4.98 billion by 2021.



We also investigated "bull" and "bear" market segments and found for bullish growth that the aseptic prefilled syringes segment is growing at an exponential rate with no signs of slowing down. Currently, around 3.5 billion prefilled syringes are produced each year and that number is growing between 9%-10% annually. The *Future of Alliances and Partnerships in the Prefilled Syringes Market to 2020,* forecasts that the global market for prefilled syringes will hit $6.6 billion in 2020[9]. The value of the market is estimated to reach $7.9 billion by 2024. As for the bearish segments, with SUS processing on the sharp growth rise, this methodology will largely displace stainless steel equipment from the PDMS space altogether in the next 5 to 10 years.

For further in-depth reporting we can request the market research services of our affiliates but this will be at an additional price of $800 to $1000 depending on the scope and stratification of data required.

8 https://www.businesswire.com/news/home/20170522005783/en/Global-Pharmaceutical-Packaging-Market-North-America-- Accessed August, 2019

9 The Future of Alliances and Partnerships in the Pre-Filled Syringes Market to 2020, Smithers Rapra, http://www.smithersrapra.com/market-reports/medical/the-futureof-alliances-and-partnerships-in-the-pr Accessed July, 2019.

Key Take Home Points

- *The client's packaging production infrastructure needs to transform from manual to continuous automated production lines. This infrastructure should also incorporate just in time (JIT) and continuous improvement (CI) elements in manufacturing single use system (SUS) packaging components. Human resource management should hire experts from stable sterile formulation design, sterile packaging QC, cGMP specialist areas as well as industry leaders in sterility material science, process engineering and production technology. The innovative packaging technologies strategic business unit (SBU) of the organisation are tasked with designing and developing SUS solutions that will meet component compatibility, scalability, sterility, biocompatibility, eco-sustainability, hybrid systems & quality-by-design (QbD) flexibility needs and to incorporate unique technology features in those packaging products. The procurement of primary packaging material SBU of the company needs to have in place high-tech. procurement systems for deriving cost savings, process improvement, supplier innovation, optimum price negotiation and contractual terms.*
- *The threat of new entrants and the bargaining power of raw material suppliers was recognised as being low. However competition is coming from the threat of packaging product substitutes and the high bargaining power of biopharmaceutical manufacturer buyers of Drug A packaging material. Low and high profitability scenarios using Porter's Five Forces were presented, and the client is urged to focus on those critical factors that will yield high profitability.*
- *Among the high value differentiated (HVD) products surveyed, for single-use bioreactor media containers, the client's transfer capability into this market segment is low, whereas the profitability is high. Stopgaps cited for this product are: gaining marketing approval, acquiring validation of compliance and acquiring the necessary global logistics and distribution networks. For ready-to-fill and port bag containers, these products represent both a high transfer capability and profitability for the client with stopgaps of biocompatibility, acquiring marketing approval and validation of compliance. Clean rapid transport ports (CRTPs) are noted as a medium transfer capability opportunity but with low profitability furthermore there are stopgaps of low return on investment, along with marketing approval and validation of contamination control challenges. Closure processing systems (CPS) represent a low transfer capability yet a high profitability. Stopgaps noted are: stringent physico-chemical and biological testing required to meet sterility and safety standards and acquiring marketing approval. DPTE (in French: Double Porte pour Transfert Etanche) beta containers were revealed as a low transfer capability and medium profitability product with stopgaps of: the design of the container to cope with high productivity targets, production throughput and hence in transfer operations; the stringent security (interlocking between isolators/restricted access barrier systems (RABS)) requirements, both for the transfer port user and for the transfer itself; greater emphasis on ergonomics, driven by the evolution of labour legislation around the world to protect operators from musculoskeletal disorders. Glove leak and transfer leak testers (GLTs & TLTs) are low transfer capability but high profitability products, with the stopgaps being: stricter preventative maintenance programs and new glove or sleeve (gauntlet) assembly technology being introduced; the choice of durable glove materials, minimises the need for GLTs & TLTs. Isolators would be a low transfer capability and medium profitability market for the client with stopgaps noted as: biopharmaceutical manufacturers switching to RABS due to affordability and flexibility. Aseptic prefilled syringes are a high transfer capability product opportunity for the client albeit deriving low profitability. Stopgaps for this product are: the numerous key providers in this*

segment; small filling volumes requirement putting demand on all production areas, including process design, technical equipment, and packaging material. Transdermal patches and on-body devices and implantables represent low transfer capability yet high profitability products. The stopgaps are: a long anticipated regulatory approval timeline and the patient training and education requirement as an additional logistical and cost hurdle.

- *The critical success factors for the client to become a "market winner" in the PDMS space are: flexible packaging and development, providing an automation solution, implementing single-use systems as a packaging solution, implementing QbD elements into the packaging products and developing patient-centric packaging solutions.*
- *By strategic group analysis, the following sets of competitors were found to offer respectively their strategic set of product and services to SUS drug manufacturers: Company Y & Company Z – offers SUS packaging to cater for buffer solutions and cell-culture media production; Company S & Company W – provides SUS packaging for end to end scalability; Company Z & Company W - offers SUS packaging compatibility between single-use systems; Company S - packaging accommodates for hybrid process design; Company S & Company Y - SUS packaging demonstrates end to end biocompatibility; and Company S- acquired validation status as an SUS packaging supplier.*
- *Feasibility studies were conducted on ultraclean, rapid prototyping, material & design expertise and trouble-shooting services, as to whether such a service would be feasible to develop as a SBU. From the client's perspective of its current operational and financial position, all services were graded as medium feasibility for development as a SBU in the PDMS space with the exception of material & design expertise that was assessed as a high feasibility SBU.*
- *Although the outcomes of a go/no-go analysis for the development of CRTPs, CPSs, DPTE beta containers, GLTs & TLTs and Isolators were all no-go, upon access being granted to the client's financial statements and financial planning reports, these findings should be analysed for further refinement and recommendations put forward accordingly.*
- *The short term "disruptors" for 2022 using the six macro-business PESTLE framework (political, economic, social, technological, legal and environmental) will be: political – a no-deal Brexit; economic – rise of packaging material prices imported from/exported to China until a new US-China trade agreement can be ratified; social - raised consumer expectations regarding packaging formats and features; technological – Drug A manufacturing demanding fast changeovers between different packaging containers with robotic control the only way to cope with this production design; legal – a large volume of bio-generics and bio-similars impacting on regulatory authorities to impose stricter cGMP guidelines; environmental - pressures from environmental lobbyists to justify the high turnover of raw materials needed in SUS based Drug A manufacturing and packaging.*
- *The key markets and products needed for heightened focus in the PDMS space are: HVD packaging products for SUS based biopharmaceutical manufacturers, on-body devices and implantables, HVD packaging products offering flexibility, scalability and assured sterility of Drug A manufacturing, incorporation of smart raw material into the packaging products and acquisition of strategic partnerships with pharma and contract development manufacturing organisations (CDMOs) for sourcing of appropriate raw materials and the final packaging formats.*