Exploring the Use of the World Health Organization Total System Effectiveness Approach and Market Opportunity Navigator to Identify Initial Positioning and Targeting of a New Bioneedle™ Delivery Technology for Vaccine Administration

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ABSTRACT

With the advent of COVID-19, the vaccine industry has gained much attention. Increased focus on vaccines, vaccine delivery methods, and vaccination campaigns has led to the need for more efficient strategies to evaluate product positioning and targeting of new delivery technologies. This qualitative exploratory study examines how Bioneedle Drug Delivery (BDD), a European-based firm developing a needle-free vaccine delivery system, addresses these considerations. It specifically examines how BDD 1) positions its Bioneedle™ platform vs. other non-needle vaccine delivery systems (in market or development) using the World Health Organization's Total System Effectiveness Approach and 2) targets its lead indication for use using Market Opportunity Navigator for entry in a crowded market. Such efforts lead to a positioning statement for BDD's new platform to identify lead customers and opportunities, key competitors, and points of differentiation. The output from this initial exploratory work leads to a path for future study to assess the relative positioning and targeting of this technology more rigorously within the highly competitive vaccine landscape.

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INTRODUCTION

The rise of the Coronavirus Disease 2019 (COVID-19) pandemic has pushed for rapid technology development and generated impressive revenue streams within the vaccine market. Pfizer's COVID-19 vaccine generated $36.8 B in sales in 2021, officially making it the top-selling pharmaceutical product in history for a single year.[2] Analyses estimate the global vaccine market size at $56 B US dollars, a number projected to rise even more in the coming years due to the pandemic increasing awareness of a global need for more innovative vaccine development.[1] The needle-free (NF) injection system market exists as a smaller segment within the entirety of the vaccine market. One can further segment this subcategory of the vaccine marketplace into pre-filled vs. fillable NF injectors. The latter segment dominates the field and has the largest market share of 57.2% as of 2020.[2] The global NF injection system market is valued at $31.2 B in 2022, with projections to reach $94.1 B by 2028.[2] In this space, frontline companies focus on product innovation, mergers and acquisitions, joint ventures, collaborations, and partnerships to drive their continued market strategy to conquer common issues of today's vaccine administration process such as waste considerations (Figure 3), storage, and speed of administration.

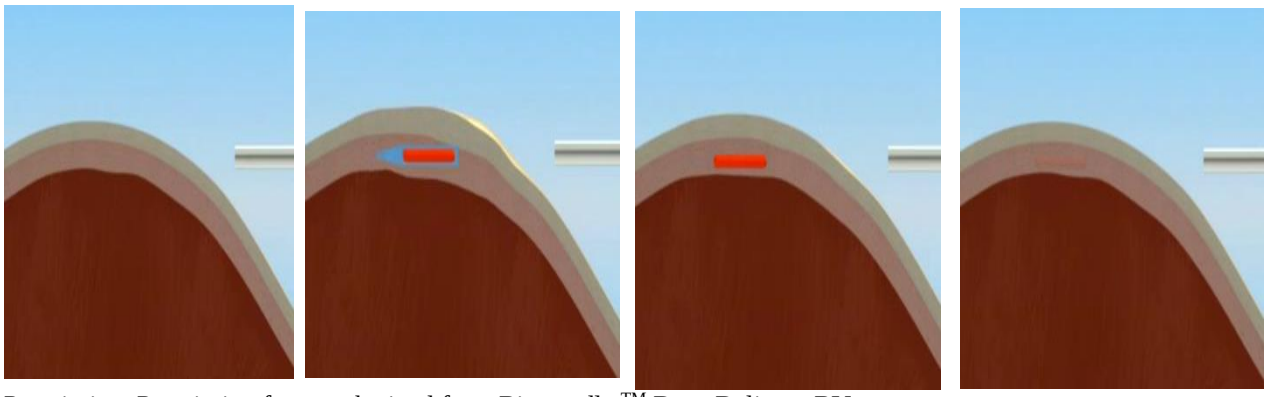

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Figure 1. Bio needle™ Administration[3]

Figure 2. Vaccine Cold Chain Cycle[8]: The progression from manufacturing through end-user delivery

Bio needle Drug Delivery (BDD) is a Netherlands-based biotechnology company advancing a vaccine delivery platform to replace traditional plastic syringes, needle canons, and associated waste. A Bio needle™ is a biodegradable, needle-shaped mini-implant. Manufacturers can pre-fill the Bio needle™ with injectable medications to ensure rapid, pain-free delivery (Figure 1).

Vaccines formulated in a Bio needle™ remain thermostable, eliminating the cold chain's cost and supply chain issues (Figure 2). However, BDD's challenges include building global partnerships for its current platform and gaining available capital to forward its clinical development program. They have completed preclinical trials in tetanus toxoid, hepatitis B, influenza, and inactivated polio vaccine (IPV). With limited funding to advance its clinical program, BDD must define its competitive space.[3]

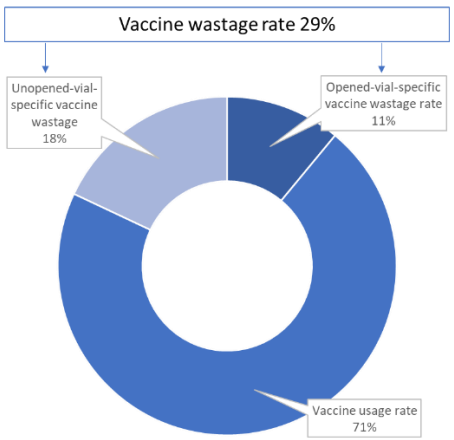

Figure 3: Visual depiction of the relationship between usage rates, vaccine-related waste, and vaccine vial-specific waste from Monitoring vaccine wastage at the country level: Guidelines for program managers[15]

This qualitative exploratory analysis addresses four objectives to evaluate BDD's competitive position and future opportunities. The first aims to determine how the Bio needle™ compares to other non-needle vaccine delivery devices. The next focus is on how BDD could best position its Bio needle™ for entry in a highly competitive, densely populated market. This effort enables BDD to target the Bio needle™ by defining lead opportunities for development and commercialization. Finally, it highlights the need for further empiric investigation to define the optimal place for the Bio needle™ product within today's highly competitive vaccine and delivery system landscape.

METHODS

Product development processes usually follow a traditional flow pattern involving stages of research and development, assessing global supply and applicable policies, and estimating uptake by regions or specific markets (Figure 4). Identifying unmet needs in target markets to provide a more detailed focus guides opportunity scanning, identification, and development. This study approached market and strategy opportunities using a dual method involving the World Health Organization's (WHO) Total System Effectiveness (TSE) Framework and the Market Opportunity Navigator (MON). This study employed the WHO Total Systems Effectiveness Framework (Table 1) for comparative assessment and positioning. It also used the MON (Figure 5), a proprietary tool, to evaluate and target market opportunities most appropriate for Bio needle™ to pursue.

WHO TSE Framework

This framework measures and evaluates identified competitors. The World Health Organization developed it to answer the driving question: "How can entities evaluate the potential of innovative vaccine products and technologies in resource-constrained settings?" The answer: a total systems effectiveness approach to decision-making. The TSE framework evaluates vaccines and their attributes from a systems perspective to compare the value of each product in different settings. Additionally, it incorporates the country's perspective when deciding about vaccine introduction and changing products. This consideration allows countries to use the framework and their local data to compare and analyze tradeoffs between current and pipeline products.

Research has shown that the TSE works best using a workshop-style approach as it helps to foster better discourse around country needs and clarifies tradeoffs between product characteristics that are acceptable from the perspective of stakeholders. The framework involves two main categories: impact and cost. Those two categories segment into the areas of health impact, coverage, safety, commodity cost, and vaccine delivery cost (Table 1).[4]

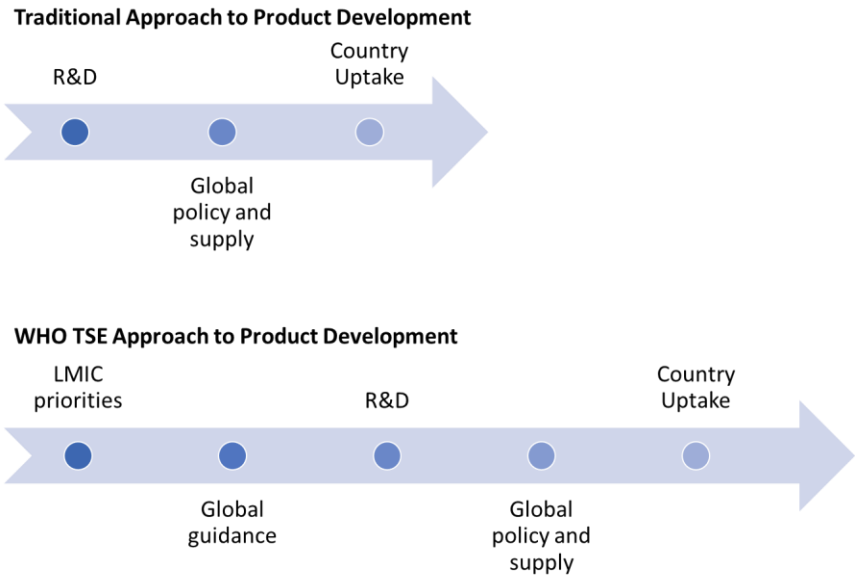

Figure 4. Approaches to Product Development[6]

Table 1. Total Systems Effectiveness Framework[6]

TSE Component		Description
Impact	Health Impact	To what extent does the vaccine presentation protect against disease? Indicators: Efficacy; effectiveness; factors affecting potency and timeliness of vaccination; duration of protection
	Coverage	How does the vaccine presentation affect the proportion of the target population receiving the full vaccination schedule? Could the vaccine presentation decrease equity gaps in immunization? Indicators: Incremental coverage, improvement (indicated by vaccination schedule, storage requirements, administration requirements, acceptability, doses per container)
	Safety	Does the vaccine presentation have a lower safety risk? Indicator: Adverse events following immunization (AEFI); risk of programmatic error (incorrect preparation, contamination, incorrect delivery, needle-stick injury)
Cost	Commodity Cost	What is the cost of the vaccine and supplies for complete vaccination, factoring in wastage? Indicators: Vaccine cost, delivery technology cost, safety box cost
	Vaccine Delivery Cost	What are the operational costs of delivering the vaccine? Indicators: Storage cost, transport cost, administration cost, waste disposal cost, monitoring and evaluation, introduction cost (including training, storage expansion, social mobilization/communication)

TSE: Total Systems Effectiveness

Using the TSE framework, this analysis conducted open internet research based on relevant companies' pipelines and needle-free injection. This effort identified the main competitors within the space: Crossject, Enesi, Gamastech, Inovio, Pharmajet, and Takeda. The TSE analysis evaluated these companies' technologies based on thermostability, pain level, administration time, dose sparing, and reduced waste in creating a competitive matrix.

MON

Marc Gruber, Ph.D. and Sharon Tal, Ph.D. created the MON to assist in driving forth business decisions when there are market uncertainties that entrepreneurs need to prioritize and consider. With limited funds to pursue a breadth of indications, startups need to focus and strategically develop their products for the most receptive market. This tool's premise is that for a product to have a successful launch, it first needs to have a defined, specific market where it meets customer demand. The MON consists of three steps: market opportunity set, attractiveness map, and an agile focus dartboard (Figure 5). The market opportunity set is the first brainstorm of the technologies' key strengths and customers who may benefit from the technology when implemented.

The next step engages the attractiveness map. This piece compares the potential and the challenges associated with the desired opportunity areas. It also addresses specific questions such as: Where is a quick win? Where will we face the most challenges? The final step engages an agile focus dartboard to prioritize opportunities for short-and-long-term strategies for growth.

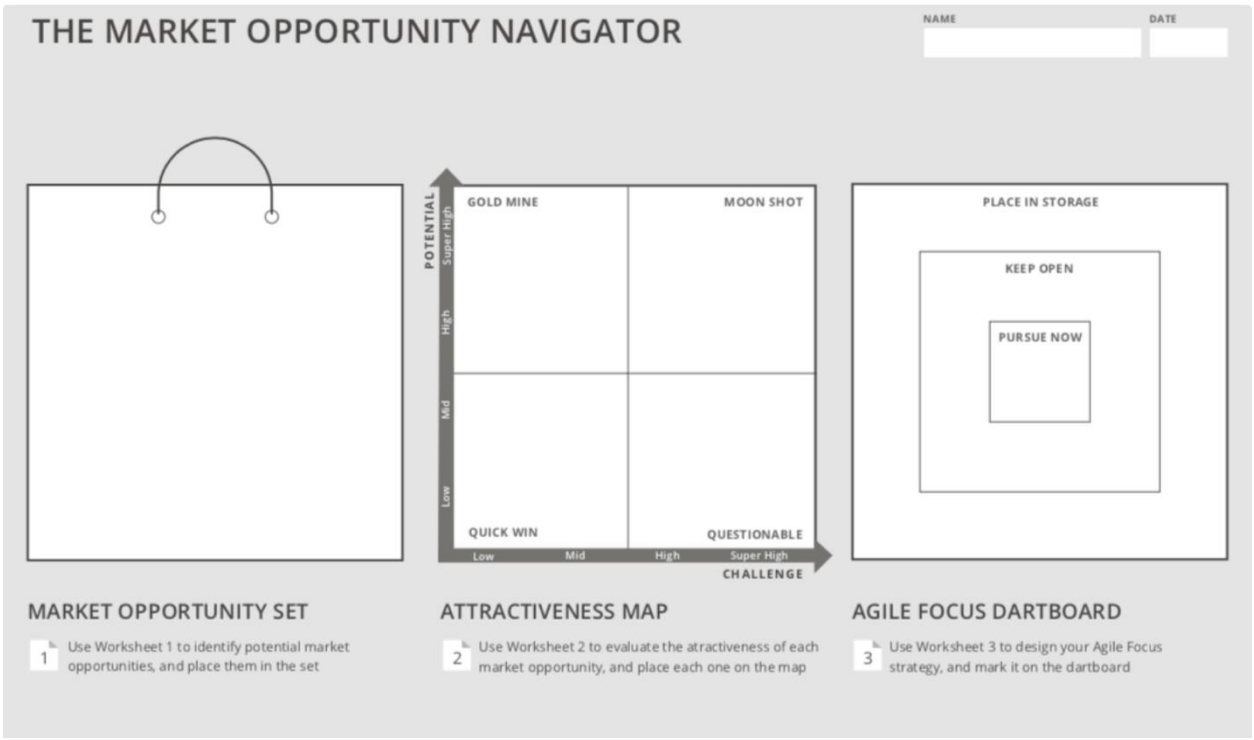

Figure 5. The Market Opportunity Navigator Worksheet[7]

Figure 6. Market Opportunity Navigator: Worksheet[7]

The "worksheets" (Figure 5) are the input sheets for each step. The Attractiveness Map inputs sheet involves inputs to evaluate both the "potential" and the "challenge" that each opportunity holds for the technology of interest (Figure 6). After evaluating each opportunity for its potential (reasoning for purchase, market volume, and economic viability) and the associated challenges (obstacles for implementation, development time and delay to revenue, and external risks), this effort arrives at overall potential and challenges ratings for each opportunity that the technology of interest, Bioneedle™, might face within the greater setting for further development.

RESULTS

This study's findings facilitated an understanding of the market that the Bioneedle™ of three critical areas. The first involves the market to enter. Second, the theoretically most suitable opportunities for BDD to engage in future clinical development. Finally, a positioning statement that these findings and outlook informed.

Table 2. Competitor Analysis Matrix

	BDD[5]	Crossject[9]	Enesi[10]	Gamstech[11]	Inovio[12]	Pharmajet[13]	Takeda[14]
Thermostability	Yes	No	Yes	No	Yes	No	No
Pain Level	Low/none	Normal	Low/none	Low/none	Low	Low/none	Low
Time to Administer	0.5 ms	<0.1 sec	< 20 sec	< 4 sec	Rapid*	< 0.1 sec	0.35 sec
Dose Sparing	Yes	Increased	Yes	Increased	No	Increased	Increased
Reduced Waste	Yes	No	Yes	Yes	Yes	No	Yes

*Rapid is a claim made by Inovio. The analysis did not find an exact time measurement.
ms= millisecond; sec= second.
BDD: Bioneedle Drug Delivery

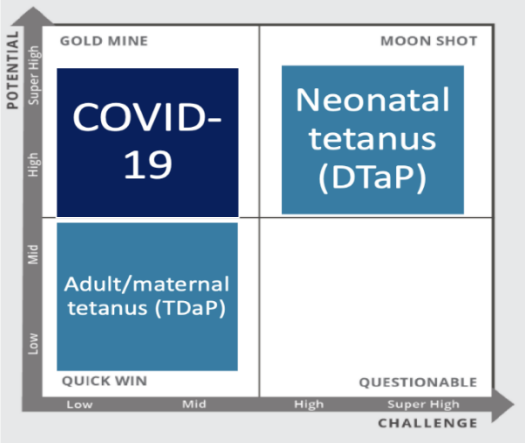

Figure 7. Attractiveness Map

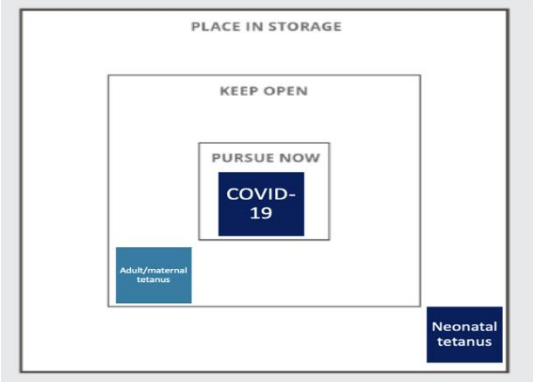

Figure 8. Agile Focus Dartboard Results

The TSE framework generated an idea of the current market landscape, focusing on key comparators and informing the dispersion of the market and its gaps (Table 2). The generated comparative matrix offered a side-by-side review of the core competitors BDD would be facing when it launches its lead product, including Crossject, Enesi, Gamastech, Inovio, Pharmajet, and Takeda. Key elements within the matrix related to this investigation include the quality of thermostability as exemplified by Bioneedle™, Ensi, and Inovio, but not other competitors. Bioneedle™ and Ensi, but not the remaining competitors, exemplify the quality of dose-sparing technology. Other considerations such as pain level, administration time, and waste reduction showed a move even mix of other attributes between competitors. When considering the full panel of results, investigators observed that the holistic profile of Bioneedle™ provided a strong profile compared to the basket of key competitors.

The MON delivered an idea of the remaining unmet need or areas of remaining room for development. The investigative team uncovered key focus areas contextualized by their potential and associated degree of developmental and launch challenges (Figures 7 and 8). In the Attractiveness Map, the development of the neonatal Tdap (tetanus-diphtheria-pertussis) would offer both a high degree of potential benefit and a high level of risk and potential developmental challenge, while adult Tdap development would offer less in both metrics (Figure 7). However, pursual of the COVID-19 development pathway would offer a very high potential for development with much lower associated risk and challenges. This figure

depicts these opportunities as types of "wins" which range from "moonshot" to "quick win" for DTaP development but places COVID-19 development as the "gold mine" opportunity. The next action is to carry these findings into the Agile Focus Dartboard, where we then find the call to immediately pursue the COVID-19 vaccine development pathway well within the "immediate" development recommendation category (Figure 8). The effort here suggests that the adult Tdap be "kept open," and the neonatal Tdap is "placed in storage" based on their benefit-risk profiles for further development.

Table 3. The Emergent Bioneedle™-Specific Positioning Statement

Positioning Statement Element	Specific to Bioneedle™
For Whom:	Developing economies' governments
Problem to Solve:	Increased access to safe, effective, and affordable vaccinations to protect from COVID-19
Our product includes:	Bioneedle™, a device
That:	Allows for rapid, effective, and thermostable vaccine delivery
Unlike:	Enesi and PharmaJet
Ours:	Eliminates plastic and biohazard waste, does not require cold chain monitoring, and is 160x smaller to transport and store

The research from the TSE and MON led to a positioning statement for Bioneedle Drug Delivery (Table 3): For developing economies' governments who need increased access to safe, effective, and affordable vaccinations to protect from COVID-19, Bioneedle™ offers a device that allows for rapid, effective, and thermostable vaccine delivery. Unlike competitors, such as Enesi and PharmaJet, Bioneedle™ eliminates plastic and biohazard waste, does not require cold chain monitoring, and is 160x smaller to transport and store. Bioneedle Drug Delivery will launch best in an economy that brings significant challenges to the difficulties of today's vaccine administration. Such issues include cold chain and storage. Efforts should target the countries most impacted. A Bioneedle™ should position itself against comparator products by focusing on its unique holistic profile. It can offer plastic and biohazard waste elimination and be easy to transport and store.

DISCUSSION

The global vaccine market is an attractive industry as it grows and has gained more attention since the COVID-19 pandemic. The pandemic pushed for rapid technology development and opened many conversations about the inefficiencies and inequality of current vaccine distribution. The current vaccine market still faces an immense unmet need in facing challenges associated with syringe, needle, vial, and refrigeration (SNVR) considerations, administration, cold chain stability, immense waste generated, and global vaccine inequity.

As small biotechnology and larger pharmaceutical companies attempt to tackle these issues, a competitive analysis brings an inherent bias when comparing one's product with other competitors. Unlike standard competitive analyses, the team decided to utilize the WHO TSE framework as an alternative approach. This effort enables the evaluation of innovative vaccine technologies from a systems perspective. Compared to traditional competitive analysis, this gave a greater view of what different systems prioritize when evaluating biotechnologies such as waste, cost, and/or the cold chain needs, which allowed us to position Bioneedle™ for developing economies' governments where its strengths are most sought after. Because infectious diseases do not equally affect each country, it is imperative to ensure that comparative analysis of technologies does not miss such factors. This consideration led this effort to move away from using a traditional landscape grid or perceptual map. Currently, no study has evaluated the differences between pipeline products using the TSE. This paper provides an opportunity for further research into this evaluation method for products as they prepare to enter the market.

Because a Bioneedle™ is a drug delivery device, it has the advantage of multiple opportunities to enter the market with different vaccines. Amid the COVID pandemic, an mRNA vaccine seems valuable, considering the amount of research and investment opportunities in this market. Many other options still need consideration during this time. One example is emphasizing disease states ignored as the world focuses on coronavirus. This effort allowed the use of the MON to position BDD. While COVID-19 is an obvious key opportunity, it is also a competitive space. Utilizing the MON approach allowed the team to introduce Bioneedle™ to other available markets, such as tetanus. While tetanus has not had as much attention as COVID, it is still a major unmet need in infectious disease and could be a place for Bioneedle™ when it wishes to expand into other markets in the future. In a previous case study utilizing the MON, York and colleagues described in *Market Selection for MyoTecSci: How to Decide "Where to Play" from Multiple Options.*[16] This current work confirmed the need to understand and evaluate each marketplace for a company to have the best strategy and direction moving forward.[16] When life science startups do not know their target market, they cannot efficiently

allocate the funds needed for research and development to bring their products to market successfully.

Before BDD can properly decide where to enter the market, it is imperative to partner with vaccine manufacturers to conduct further clinical trials to prove their advantages over the traditional needle and syringe method. This exploratory research's contribution is an analysis of this specific product's competitive landscape and its positioning prediction within a highly competitive market. BDD can utilize this research to lead discussions amongst their team when deciding on paths to move the business forward by having an appropriate competitive analysis and understanding of their lead indication. Additionally, the findings from this research will impact other emerging technologies by defining a path for evaluating future opportunities and the relative competition.

LIMITATIONS

Like other research, limitations do exist. First, this study was a qualitative, exploratory investigation. Accordingly, this effort did not perform any formal sensitivity analyses during the TSE or MON assessments. As this investigation lacks such rigor, individuals should carefully interpret the qualitative analyses and related findings. The study identifies implicit bias due to the investigative team's prior exposure to BDD management. Additionally, measurement bias might exist as this investigation is qualitative. It lacks prior baseline standards to compare the metrics to inform the evaluation or the extent to which they impacted the evaluation individually without employing some form of weighting for normalization. Lastly, in concluding this investigation, the qualitative nature of this research allows for association bias to exist within the body of our conclusions. Investigators had prior exposure to the Bioneedle™ technology and team. Their pharmaceutical and biomedical backgrounds might provide more of a commercial-oriented lens around implementing new technology within a space so indelibly informed by its importance to the community and requirement for the highest reliability could have impacted the investigative team's perspective while conducting this study.

CONCLUSIONS

While the success of COVID-19 vaccinations has made exciting market opportunities for biotechnology companies, it is important to use a broad scope when evaluating competition and markets as they advance into clinical trials. When companies do not define a clear target early in their business or clinical development, it becomes difficult to focus on a unique market need and position themselves in a way that will override competitors. Utilizing the WHO's TSE approach[6] and Gruber and Tal's MON[7] allowed the team to narrow down the different criteria for success within each market to find that the Bioneedle will have the best opportunity to entrench the market. Based on our analysis, BDD should focus its efforts on developing economies' governments who need increased access to safe, effective, and affordable vaccinations to protect from COVID-19. They will need to continue market research on perceptions of their technology, innovation within the disease space, alternative funding, and competitive intelligence to ensure they have the most current information about the lead indication, relative competition, and potential partners or investors.

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