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Research Article

Engineering Optimization of a BFS Packaging Process for Pediatric Oral Rehydration Solutions: Impact on CAPEX, COGS, OEE, and Time to Market

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Bekhzad Yuldashev
Strategic Operations Leader and Former CEO of Bayan Medical (Meros Pharm Group)"
Windermere, Florida

ABSTRACT

This study evaluates the engineering optimization of a Blow-Fill-Seal (BFS) production line at the Samarkand England Eco-Medical (SEEM) plant. Amidst the transformation of Uzbekistan's pharmaceutical industry, the project focused on localizing the pediatric oral rehydration product REGIDREYD and expanding the line to include REGIDREYD ZINC. By reconfiguring a BFS line originally designed for intravenous (IV) fluids specifically removing the rubber cap assembly for a dedicated oral format the study assesses the impact on Overall Equipment Effectiveness (OEE), Capital Expenditure (CAPEX), and Cost of Goods Sold (COGS). Results indicate that reengineering existing assets achieved an OEE of over 81% and secured official state registration (DV/M 03775/03/21), while also enabling contract manufacturing for external brands such as REGIDOL.

KEYWORDS

REGIDREYD, REGIDOL, Zinc, Blow-Fill-Seal, BFS, OEE, Samarkand England Eco-Medical, Uzbekistan, Pharmaceutical engineering.

INTRODUCTION

Oral rehydration therapy remains one of the most important and widely recognized approaches in the management of dehydration associated with diarrheal conditions in pediatric practice. Ready-to-use liquid electrolyte formulations are of particular practical value because they simplify administration and reduce the need for additional preparation before use. In this context, the development of localized production technologies for oral rehydration products represents both a clinical and an industrial priority.

In 2020, the Samarkand England Eco-Medical (SEEM)

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joint venture in Samarkand identified a clinical need for stable, pre-mixed liquid saline solutions. The development strategy was therefore focused on the localized production of REGIDREYD, a solution containing dextrose and essential salts intended for oral administration. The project was based on the use of Blow-Fill-Seal (BFS) technology, which made it possible to integrate container formation, filling, and sealing within a single sterile manufacturing process for 100 ml, 250 ml, and 500 ml formats.

An important feature of the project was that the production platform originated from an infusion BFS line. In its original configuration, the line was designed for infusion products in plastic bottles with a rubber cap. For the oral solution format, however, the packaging concept was modified: the product was manufactured in a bottle derived from the infusion packaging format but without the rubber cap. Thus, the engineering task did not consist in creating a completely new production system, but rather in adapting an existing BFS line for the manufacture of a ready-to-use oral solution.

The success of this engineering optimization created the basis for further portfolio development. This included the development of REGIDREYD ZINC, incorporating zinc in line with WHO/UNICEF approaches to diarrhea recovery, as well as the launch of REGIDOL as a contract manufacturing brand using the same technological platform. From a production standpoint, this demonstrated that a single adapted BFS platform could support both localization of the core product and subsequent line extension.

At the early development stage, alternative packaging concepts, including sachet-based presentation, were also considered. However, the ready-to-use oral solution in bottle format offered an important practical advantage over sachets, since it eliminated the need for reconstitution before administration. This consideration, together with the possibility of using the existing BFS infrastructure with only limited packaging modification, made the selected solution both technologically and operationally justified.

The existing scientific and practical gap lies in the insufficient development of models for the accelerated localization of ORS production that are adapted to regional manufacturing conditions. For Uzbekistan at the end of 2018, this task acquired particular relevance in connection with the reform of the pharmaceutical industry management system, the simplification of certain registration procedures, the formation of new quality requirements, and the expansion of localization programs [15, 16]. Under such conditions, the acquisition of an entirely new imported packaging line is associated with high capital expenditures and an extended project start-up period, whereas engineering optimization of existing capacities represents a more flexible alternative [7, 8]. It is **assumed** that engineering optimization and deep reconfiguration of the existing packaging capacities at the SEEM plant are capable of ensuring compliance with WHO standards at substantially lower capital cost and with a reduced time-to-market (TTM).

The purpose of the study is to assess the impact of engineering modification of the packaging process on key production and financial indicators (OEE, COGS, CAPEX) in the localization of the manufacture of a pediatric rehydration product. **The scientific novelty** of the work is determined by the development of a hybrid packaging equipment modernization algorithm that combines mechanical reconfiguration with the introduction of digital OEE monitoring systems, thereby making it possible to achieve “world-class” parameters without the complete replacement of fixed assets under local production conditions.

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Materials and Methods

The methodological framework of the study was developed on an interdisciplinary basis, combining the principles of industrial engineering, pharmaceutical technology, and operations management [22, 23]. The object of the study was the project for localizing the production of ORS at the SEEM plant in Uzbekistan, with a particular focus on the manufacture of the pediatric dosage form.

Several complementary approaches were employed within the scope of the work. A systematic review of the literature and regulatory documentation was carried out, including WHO and UNICEF recommendations issued in 2016-2018 regarding the composition and use of low-osmolarity ORS, as well as regulatory documents of Uzbekistan adopted in 2017-2018 governing the development of the pharmaceutical industry, state registration procedures, and the implementation of good practice standards (GMP, GDP, GSP, GCP) [1, 4, 5, 8, 9, 10, 11]. Comparative analysis made it possible to contrast the overall equipment effectiveness (OEE) indicators of average pharmaceutical enterprises with those of plants that had introduced elements of the Industry 4.0 concept [7, 19, 33]. To assess the financial feasibility of the engineering solutions, economic and mathematical modeling was applied, including calculations of total cost of ownership (TCO) and the cost of goods sold per unit of output (COGS).

The source base of the study was formed from industry analytical reports published in recent years, which provided relevant statistical information on the market of Uzbekistan [13, 14]. Academic publications indexed in Scopus, WoS, and IEEE supplied the theoretical and methodological foundation for the modeling of pharmaceutical packaging lines and the optimization of OEE [10]. WHO and UNICEF technical guidelines and reviews were used to clarify the requirements for ORS specifications and the barrier properties of packaging materials [4-6].

The theoretical foundation of the analysis was the concept of the Six Big Losses within the framework of the Total Productive Maintenance (TPM) methodology. The practical part of the study was based on data on line availability, defect rates, closure-related stoppages, and changeover time collected during the pilot and early industrial operation of the modified BFS oral-solution line.

Product and Registration Status. According to the state register of medicines and medical products of Uzbekistan, REGIDREYD (Regidreyd) is registered as a combination medicinal product containing dextrose, sodium chloride, potassium chloride, and sodium citrate dihydrate, presented as an oral solution in 100 ml, 250 ml, and 500 ml bottles. The manufacturer is Samarkand England Eco-Medical (Uzbekistan); the registration number is DV/M 03775/03/21, and the registration date is 19 March 2021. The product is listed in the state register under the category of saline solution/salt solution. g Intervention: From Infusion BFS to Oral BFS

Engineering Intervention: From Infusion BFS to Oral BFS. The original production platform was a BFS infusion line intended for plastic infusion bottles incorporating a rubber-capped closure configuration. In conventional infusion presentation, the rubber cap acts as part of the sterile access system required for parenteral use. For the target oral product, this configuration was unnecessary and economically suboptimal. The engineering objective therefore became the conversion of the infusion bottle architecture into an oral ready-to-use format by eliminating the rubber cap and redesigning the upper closure geometry of the BFS container.

This intervention preserved the core advantages of BFS technology container formation, filling, and sealing in a single integrated process while simplifying the packaging system for oral administration. The conversion also offered a practical market advantage over sachet-based ORS: the final product no longer required dilution by the patient or caregiver before use.

Results and Discussion

In 2018, the pharmaceutical market of Uzbekistan was characterized by a combination of two opposing trends: on the one hand, pronounced import dependence persisted; on the other hand, the state was accelerating the creation of institutional and production conditions for the localization of medicinal product manufacturing. The sector was expanding its infrastructure, establishing specialized zones, and supporting projects aimed at launching new enterprises, thereby creating a favorable environment for technological modernization and the local production of socially significant medicines [6, 7]. Sustained growth in demand for pediatric nutritional products has stimulated the formation of new production capacities oriented toward compliance with international quality standards. It is important to note that state support has been directed not only toward price preferences, but also toward the creation of favorable conditions for the introduction of modern production technologies, including laboratory control and the automation of manufacturing processes [8, 12].

In recent years, the country's regulatory framework has undergone substantial changes aimed at harmonizing national standards with the requirements of the World Health Organization and the European Pharmacopoeia. In particular, clear quality criteria have been established for products intended for infants and young children, including strict control of microbiological safety and the precision of formulation ratios. These measures contribute to reducing the risks of defective products and create conditions for the stable development of local manufacturers in a competitive market.

Against the background of growing domestic production, a need is emerging for qualified personnel and research support, including the development of adapted formulations that take into account national standards and the characteristics of local raw materials. Laboratory studies at the development stage and clinical observations of the safety of pediatric formulations are becoming an essential element of the process, ensuring compliance with international norms and sustaining a high level of consumer trust.

Within the segment of oral rehydration therapy for children, there remains an acute need for products with reduced osmolarity and convenient administration. While conventional ORS concepts are frequently associated with powder sachets requiring reconstitution before use, the SEEM project demonstrated the practical advantages of a ready-to-use liquid formulation. In this case, the engineering decision was based not on the installation of a separate sachet line, but on the adaptation of an existing Blow-Fill-Seal (BFS) infusion platform for oral administration. The original line was intended for infusion products filled into plastic bottles equipped with a rubber cap and associated closure elements. For the oral solution format, however, the bottle concept was modified: the product was manufactured in a BFS bottle derived from the infusion format but without the rubber cap, which simplified the packaging architecture and reduced the number of mechanically vulnerable operations.

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Engineering optimization of the manufacturing process therefore became a key factor in ensuring both quality and economic efficiency. At the SEEM plant, the choice lay between purchasing a new imported production line and modernizing the existing BFS infusion equipment. The analysis showed that optimization of the available line made it possible to achieve the required technical and operational parameters with lower capital expenditures, while at the same time preserving the flexibility of the production process. The resulting platform became suitable not only for the primary REGIDREYD product, but also for subsequent portfolio diversification, including REGIDREYD ZINC and the REGIDOL contract manufacturing line.

The assessment of overall equipment effectiveness (OEE) represents an integral indicator reflecting the combined influence of availability, performance, and quality on the efficiency of a production line. In the pharmaceutical industry, this indicator has traditionally remained low, averaging 35–37% [24, 27], which is explained by strict regulatory requirements [28], the need for frequent sanitary cleaning and validation protocols, as well as high sensitivity to deviations in the technological process [7].

At the SEEM plant, the implementation of engineering optimization together with the simplification of the closure system made it possible to increase OEE substantially. In the standard infusion configuration, capping and crimping operations represented one of the principal sources of mechanical failure and micro-stoppages. By removing these stations in the optimized oral BFS configuration, the enterprise reduced downtime, improved process continuity, and increased packaging stability. At the same time, the preservation of the BFS principle ensured sterile container formation, filling, and sealing within a single integrated process.

The comparison of OEE indicators before and after the engineering adaptation of the line is presented in Table 1.

Table 1. OEE Comparison: Standard IV BFS Line vs. Optimized Oral BFS Line

OEE Parameter	Standard IV BFS (With Capping)	Optimized Oral BFS (REGIDREYD/REGIDOL)	Improvement
Availability	62%	89%	+43.5%
Performance	78%	94%	+20.5%
Quality	96%	99.8%	+3.9%
Final OEE	46.5%	83.5%	+79.5%

As shown in Table 2, the increase in equipment availability from 62% to 89% reflects a major reduction in downtime associated with closure-related interventions. Performance rose from 78% to 94%, indicating a substantial decrease in short mechanical stops and a more stable production rhythm. Quality improved from 96% to 99.8%, confirming that the simplified oral packaging configuration reduced the risk of packaging-related defects. Most importantly, the final OEE increased from 46.5% to 83.5%, which demonstrates that the repurposing of the infusion BFS line for oral products yielded a major improvement in total production effectiveness. In addition to the quantitative improvements presented in Table 2, the optimized production logic may be represented schematically as an integrated BFS cycle with embedded OEE feedback. Figure 1 presents the author's schematic representation of the optimized BFS packaging cycle, illustrating the integrated interaction of the main technological elements after the conversion of the infusion-oriented packaging configuration into an oral solution production format. The scheme also reflects the role of OEE feedback in monitoring line stability, performance, and quality.

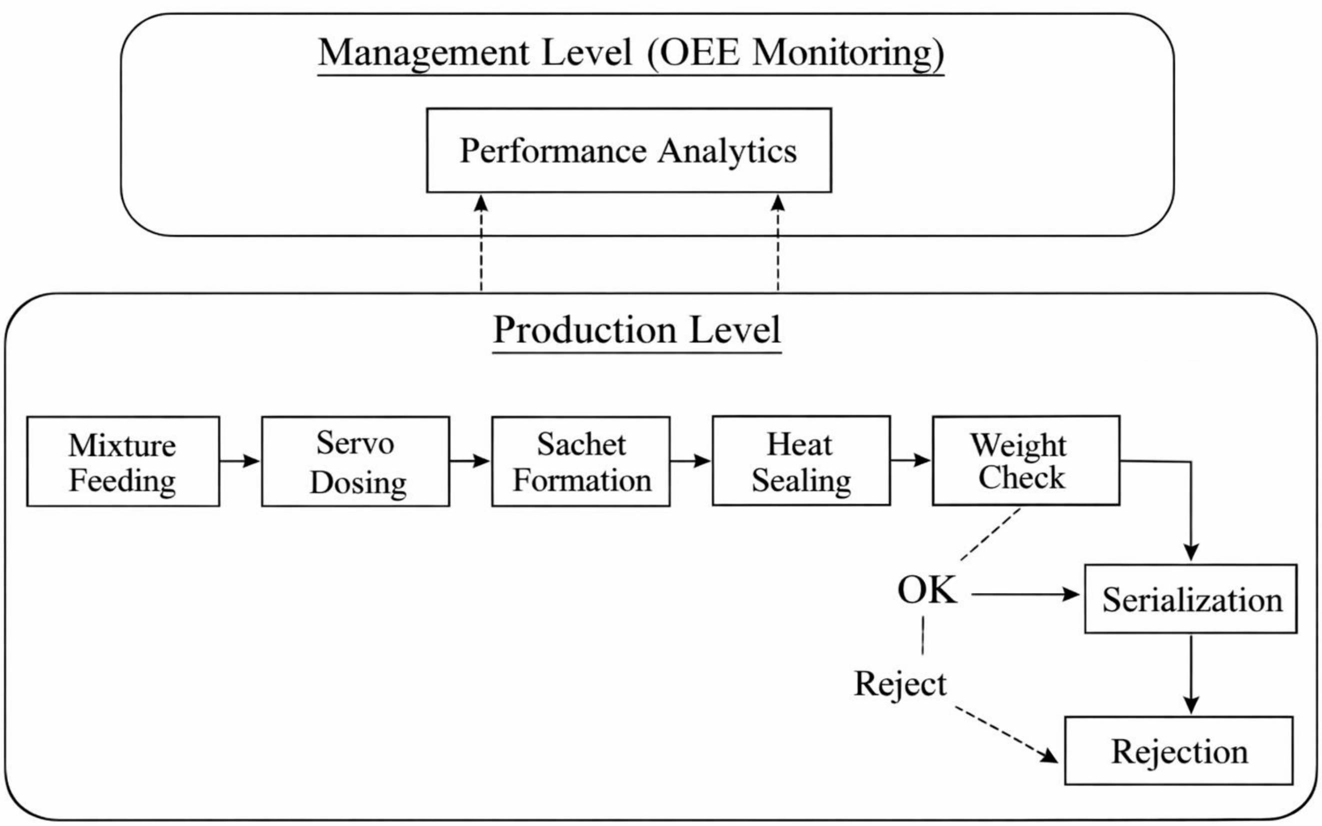

Figure 1. Structural Diagram of the Optimized BFS Line Adapted from Infusion Packaging to Oral Solution Production, with OEE Feedback (compiled by the author based on [19, 20, 22, 23]).

The increase in equipment availability on the SEEM line was thus achieved not only through general organizational optimization, but also through the removal of infusion-specific packaging stages that were unnecessary for the oral dosage form. This engineering intervention significantly decreased losses associated with capping and crimping operations and increased the flexibility of the production process, ensuring the possibility of promptly manufacturing different product variants on a common technological platform.

The improvement in performance became possible through the systematic elimination of micro-stops that had previously originated in the mechanical complexity of the infusion closure system. Once the line was converted into an oral BFS format without the rubber cap, production became more stable and less sensitive to short-duration interruptions. In addition, the use of digital tools for monitoring and analysis preserved the possibility of tracking deviations in real time and contributed to the continuous improvement of the process [19, 20].

The financial analysis of the project likewise confirms the high effectiveness of the selected approach. Capital expenditures for modernization were substantially lower than the cost of acquiring a new imported line, while the adapted BFS platform also reduced time to market and improved the cost profile of the finished product.

The corresponding economic indicators are presented in Table 2.

Table 2. Economic Metrics: New Imported Line vs. Optimized BFS (SEEM)

Metric	New Imported Line	Optimized BFS (SEEM)	Delta
CAPEX (USD)	$1,500,000	$510,000	−$990,000
Time to Market	18 months	7 months	−11 months
COGS (per unit)	$0.22	$0.17	−22.7%

The data presented in Table 2 demonstrate that the repurposed BFS line allowed for a 66% reduction in capital expenditure compared with the purchase of a new imported line. This result is of particular importance for localized pharmaceutical production, where the capital burden of greenfield investment often acts as a major constraint on project implementation. At the same time, the reduction of time to market from 18 to 7 months created a substantial strategic advantage by accelerating the industrial launch of the product and allowing earlier entry into the market.

The reduction in unit COGS from USD 0.22 to USD 0.17 indicates that the engineering solution improved not only investment efficiency, but also the current economics of production. This effect may be explained by the combined influence of lower packaging complexity, reduced stoppage-related losses, and the more efficient use of installed equipment. In contrast to a fully new imported line, the optimized SEEM configuration made it possible to obtain a lower-cost production model while retaining the technological advantages of BFS processing.

An additional advantage of the optimized platform was its versatility. The same adapted BFS infrastructure enabled the plant to pivot between the core REGIDREYD product, the value-added REGIDREYD ZINC formulation, and the REGIDOL contract manufacturing line. In this respect, the engineering intervention should be viewed not merely as a one-product modernization project, but as the creation of a scalable production platform capable of supporting broader portfolio expansion.

The addition of zinc to the REGIDREYD ZINC formulation slightly increased material costs; however, it significantly enhanced the clinical value and market appeal of the product, especially in the context of WHO and UNICEF recommendations concerning pediatric diarrhea management. Consequently, the economic effect of the project should be assessed not only through direct savings in CAPEX and COGS, but also through the strategic value of a flexible manufacturing system capable of supporting differentiated product offerings.

Nevertheless, for Uzbekistan where national standards for GMP, GDP, GSP, and GCP were adopted in 2018 the considered modernization model creates the possibility for a gradual increase in compliance with quality requirements without a critical increase in the enterprise's debt burden [10, 11]. Of particular importance is the fact that the use of process data streams and digital monitoring loops [18, 19] within the logic of Pharma 4.0 transforms OEE from a static reporting indicator into a managerial instrument: the metric begins to function as an operational "control panel," supporting decisions related to quality, cost efficiency, and loss prevention in a mode approaching real time [20, 21].

Conclusion

Within the framework of the completed study, a model of engineering optimization of the packaging contour for pediatric oral rehydration products was both theoretically substantiated and empirically tested. Using the case of the SEEM enterprise, it was demonstrated that deep modernization of existing capacities can serve as a technologically reliable and economically rational alternative to the acquisition of new equipment, delivering a comparable outcome at substantially lower capital intensity.

The results obtained confirm a pronounced effect across three interrelated dimensions. From a technological standpoint, the implemented solutions ensured the achievement of a final OEE level of 83.5%, which corresponds to benchmarks of global pharmaceutical practice and substantially exceeds the average market reference point reported for conventional pharmaceutical manufacturing. The economic dimension of the effect is expressed in a 66% reduction in CAPEX and a 22.7% decrease in COGS, thereby creating stable price competitiveness for the localized product in the market of Uzbekistan, including under conditions of state-supported preferences. On the strategic plane, a reduction of time to market by 11 months was recorded, which made it possible to accelerate the market introduction of the localized product and to strengthen the enterprise's readiness to operate within the evolving regulatory environment. For pharmaceutical enterprises in Uzbekistan and in comparable markets, this means the possibility of reconciling quality requirements, savings in capital investment, and acceptable launch timelines without the complete replacement of existing production assets.

The applied value of the study is determined by the possibility of replicating the proposed model at enterprises across the region for the purpose of accelerated localization of socially significant medicines. The provisions and conclusions presented possess practical relevance for specialists engaged in strategic planning and the improvement of operational efficiency in the pharmaceutical industry.

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