Operational Excellence by Implementation of 5S Concepts and Lean Management Practices in Vivarium

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Abstract

Modern vivarium operation requires collective efforts by cross-functional teams especially within the collaborative research organizations for the successful outcomes of comprehensive laboratory animal care program. The drug discovery with rapid screening turnovers and innovative approaches demands infrastructure expansion by increasing several other capabilities in vivarium. The strategic portfolio changes and therapeutic areas closure retained several high-end equipment's left unused that eventually occupied space in the barrier system which intricate daily operations and space management became challenging over the period. The vivarium facility was under continuous improvement by the quality assurance program based on monthly independent audit reports and compiled the compliance including animal welfare standards of at least 5 years period. Corporate initiatives such as Kaizen events, 5S concepts, Gemba walk and green labs certifications were implemented systematically at various phases across the organization including vivarium. The leadership team was a driving force behind the lean management practices and its implementation. The quality assurance program was able to bring out several improved operational processes notably by creating an additional quarantine space; repurposing high-end equipment for other investigators to support their ongoing programs; effective space utilization by creating in-house diagnostic laboratory; donating low-density animal racks for academic institutions as part of educational outreach efforts; containment of solid radioactive waste disposal by compaction process for longer half-life radioisotopes. In conclusion, lean management practices collectively demonstrated a measurable outcome in terms of continuous process improvement, effective vivarium management by ensuring compliance based on periodical observations without compromising animal welfare, conservation of energy and resources, effective space utilization and systematic implementation of 5S concepts by repurposing of equipment to other laboratories. Overall, the system-driven process has improved the standards with better performance that eventually enhanced the quality and productivity at the laboratory animal facility

Key words: *Lean Management, Quality Assurance, Kaizen Events, Gemba Walk, 5S Concepts, Process Improvements.*

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Introduction

The vivarium operations with shared facility requires effective coordination with cross-functional teams of diverse stakeholders for maintaining state-of-the-art facility in any organization. Lean management is a broad approach, considered an effective methodology for substantial productivity and is popular among many organizations (Urban, 2015). Lean is a continuous process of improvement (Camacho-Minano *et al,* 2013) and can be represented as "doing more with less" (Rymaszewska, 2014) and has to be unique for each organization (Khan *et al,* 2008) based on their nature of work environment. The lean principles were initially developed by Taichi Ohno for the Toyota Motor Corporation and coined as the Toyota Production System (TPS) for their manufacturing industries; later extended to other organizations *viz* software development, financial sectors, health care, laboratory sciences (Schweikhart *et al,* 2009) and pharmaceutical laboratories including production units (Carleysmith *et al,* 2009, Byrne *et al*, 2021). Similarly, process improvements are practiced in nonclinical (Tummala *et al,* 2014; Zynda, 2015; Okpe *et al* 2017) and clinical set up in hospitals (Young *et al*, 2001); and lean concepts are generally identifying the areas to streamline processes, reduce wastes and time between biomedical research discoveries to the clinical practices which require systematic planning within the biomedical research organizations (Schweikhart *et al*, 2009 and Gras *et al,* 2007). Lean initiatives streamline the vivarium operation and lower the costs (Stahl, 2013) without any compromise on animal welfare and compliance. Hence, continuous improvement needs several lean thinking in line with creativity that leads to innovation by adhering to principles in the drug discovery arena (Johnstone *et al*, 2011) which eventually provides positive outcomes on process excellence (Andersson, 2009) in the work environment along with team performance. The lean philosophy drive is considered a continuous process for an organization towards striving for perfection (Bhasin *et al*, 2006 Papadopoulou *et al*, 2005); several strategies for improving the efficiency and effectiveness of drug discovery and development have been explored (Hammond *et al*, 2008; Ullman *et al,* 2008; Young et *al*, 2001) and recognized the similarities apart from subtle differences in terms of lean tools applications which can be adopted across the diverse industry (Sewing *et al,* 2008). Systems thinking as an enabler for strategic decision-making processes and organizational commitments reinforces sustainability (Pandey, 2012) as well as corporate culture becomes an indispensable component (Liker, 2004) for sustainable aspects of successful outcomes. Hence, lean practice needs strong leadership; the commitment of managers is vital for lean model implementation (Dibia *et al*, 2014) and a formal approach with the strategy to focus on core elements apart from specific processes (Dickson *et al*, 2009 and Veiga 2011). Considering the need as well as understanding of existing systems, lean practices were systematically implemented to improve several processes to speed up the preclinical screening efforts across the cross-functional team at our facility.

Materials and Methods

Overview of Vivarium Operation

Syngene Laboratory Animal Research (SLAR) facility has been operational since 2009 (AAALAC accredited, GLP Certified), and infrastructure capabilities were enhanced over the period to support various therapeutic areas with space as a constraint and also a limiting factor for expansions. The animals are sourced from the approved vendors (USA/Europe/India) every week in multiple consignments which undergo stipulated quarantine (up to 21 days) before release into the holding areas for experiments. The high turnover of incoming animals and stringent quarantine period was always a concern and widely discussed among team members on various forums. To increase the housing capacity, low-density conventional racks were replaced by Individually Ventilated Cages (IVC) within the

available space. Over the years, many systems were introduced to reinforce the capability enhancements such as Quality Assurance, Kaizen events, 5S concepts, Green lab certifications, Gemba walk, Colony management software development, Automation for vivarium decontamination, and Radioisotope waste disposal by compactor method was implemented in various phases along with several other tools as part of the continuous improvement process.

Quality Assurance Program

The quality assurance within the veterinary science function plays a pivotal role in overseeing the regulatory process, system implementation, and animal welfare aspects which is considered an integral part of operations and management. In addition, periodical monitoring of approved protocols, animal welfare standards, process improvements, and facility infrastructure development also part of the system. Based on monthly compiled observations, the impact assessments along with possible suggestions were communicated to management, facility veterinarians, and animal care supervisors to rectify observations and/or concerns if any to meet the compliance.

Implementation of 5S concepts

The 5S concepts were introduced systematically with initial awareness sessions by identifying representatives from each functional area within the vivarium. The 5S (Seiri, Seiton, Seiso, Seiketsu, Shitsuke in Japanese) represents Sort (go through all items and dispose of those not needed); Straighten (create a place and labeling of each item); Shine (keep everything clean); Standardize (develop systems to monitor above three steps); Sustain (use management audits to maintain adherence and sustain gains) in workplace to improve efficiency levels of entire process. Strategy brainstorming sessions followed by stakeholder meetings were conducted with the following objectives such as identification of unused materials (non-value-added items), space marking to store segregated materials with “Red Tag” labeling, and repurposing of equipment to different functions within the facility as well as outside institutions.

Kaizen Events

The kaizen event (kaizen means “improvement” or “change for the good” in Japanese) was aimed to replace, reduce, and refine the use of animals for research as the central focus. Many cross-functional team members were actively engaged in the planned meetings and discussed various aspects by adhering to 3R’s principles (Replacement, Reduction, Refinement) to improve existing practices. The primary aim was to validate current value stream maps, identify the pain points, prioritize solutions based on benefit *vs* effort (low, medium, and high impacts as measurable scale), and develop a plan of action for each identified point. The overall exercise was aimed to reduce 15% animal usage without compromising science and any impact on the ongoing research as per the timelines. However, the management was emphasized by decreasing animal consumption thereby increasing efficiency along with the associated benefit of reducing cost, enhancing awareness of animal welfare, creating animal holding capacity, increasing the equipment life along with several other thought processes about study design which includes alternative methods and other mechanisms which were implemented.

Gemba Walk

The Gemba walk (“Gemba” means “the real place” in Japanese) was initiated by the senior leadership team and laboratory managers also part of the quarterly visits or as and when required to “go and see” the workplaces and observe the practices without affecting ongoing experiments. The observed points were discussed based on priority and feasible solutions implemented step by step towards process improvements and subsequent visits made to visualize the progress apart from written procedures such as guidelines or Standard Operating Procedures (SOP) are in place. The above visits aimed to reinforce the

centralization of resources wherever applicable to facilitate easy access for all the users and create space for future purposes.

Green Lab Certifications

As part of the annual evaluation process (platinum, gold, certified, aspiring categories), successive certification was assessed from 6 functional areas within the vivarium. The online scorecard survey was aimed to reflect the opinions and views of team members who have shared resources in animal facilities represented by a team member while on assessment to complete the survey. In general, the evaluation was carried out by considering potential opportunities such as administration, process control, energy conservation, waste management, and communication aspects from each functional area and collated further.

Colony Management Software

The import of laboratory animals was increased over the period and necessitated for integration of the functional domains to develop a custom data management software "Lab Tracks" (Locus Technologies - USA) based on the facility requirements. The software offers traceability of animal numbers from quarantine to experiment completion, and animal usage against each approved protocol to meet the statutory and regulatory requirements. The software provides online tracking of inventory and real-time protocol status also be viewed by the user groups. In addition, the animal utilization was maintained and able to be retrieved by the stakeholders as part of the facility documentation and submitted to the Institutional Animal Ethics Committee (IAEC) by meeting the requirements.

Automation for Vivarium Decontamination

The facility is built with clean room panels and each Heating Ventilation and Air Conditioning (HVAC) unit was hooked to at least 4-6 animal and/or procedure rooms which prevented individual room decontamination and if any HVAC was shut down, it eventually affected the neighboring rooms. Considering the inherent complexity, an automation process was developed by creating the bypass ducting by isolating individual rooms which can be operated by the in-house developed Supervisory Control and Data Acquisition (SCADA) software system. Additionally, vaporized hydrogen peroxide and chlorine dioxide systems operations were integrated with custom software for routine decontamination.

Radioisotope Disposal by Compactor Process

The central radioisotope research laboratory was used by multiple investigators for their *in vitro* and *in vivo* experiments. Over the period, it was learned that disposal of long-lived radioisotopes became a challenge and occupied lots of space at the central waste disposal pits located within the facility premises. To overcome the issues, an electrically operated compactor was fabricated by the engineering team which ideally compacted solid radioisotope wastes before disposal into the dedicated pits.

Results

The management has implemented several lean practices over the years as part of system improvements (**Figure 1**). The initial infrastructure of capital equipment and modernization of high-density cages resulted in increased animal holding capacity from 7500 to 18500 animals as averaged after the vertical expansion with available space that leads to parking of many unused racks in the buffer animal rooms and/or corridors (**Figure- 2**). However, kaizen event analysis with 22 identified potential options revealed the possible benefits (Low 6: Medium 12: High 4), and corresponding efforts (Low 11: Medium 6: High 5) were devised by stakeholders upon compilation (**Table - 1**). A total of 34 different rodent strains were analyzed from all the animal users and confirmed that 95% of consumption was linked with planned studies except for the rest of the animals ordered by anticipating the test compounds. Subsequently, lab track software development offered online tracking of all the protocols by investigators proactively verifying their animals and

transferring them to another protocol for better utilization and/or repurposing by other investigators. The online scorecard evaluation of green lab certification results averaged platinum (1), gold (4), and certified (1) categories of at least 3 consecutive years. The Veterinary Science Quality Assurance report compilation (326 observations) based on monthly audit reports of at least 5 years period was categorized into animal welfare and research protocols (43); facility infrastructure (52) and process improvements (231) within the vivarium (**Figure-4**). However, the Gemba walk findings showed many processes covering infrastructure, and safety capabilities including the refrigerator units for two years provided a scope to deploy 40% of refrigerator units and made them available for repurposing to other users. In addition, a space for a central diagnostic laboratory is an additional capability for the timely screening of samples for animal health monitoring purposes. The automation of the decontamination process resulted in the flexibility to provide for at least 4 rooms/areas on any given day without affecting the neighboring areas. The evaluation of facility fumigation data showed that 146 and 86 cycles were performed in the subsequent two-year period out of 340 target cycles. The corresponding automation after validation had enhanced the decontamination aimed to cover up to 510 cycles/year thereby increasing 66% by the additional capability to accomplish all the targeted cycles within the timeframe. The 5S implementation enabled the identification of materials (246 unused items), especially from neuroscience and obesity therapeutic areas which included high-end clinical chemistry auto-analyzer, Comprehensive Laboratory Animal Management Systems (CLAMS), and a variety of pain-related equipment including many other behavioral instruments that occupied the space in the rooms **(Figure-3**). In addition, low-density racks (40 units) along with cage-set accessories were segregated under red tag items and some of them were modified for reuse (**Figure-5**). The mobilization of resources, transfer of equipment along with the exchange of space resulted in an increase of quarantine holding capacity by up to 25,000 rodents per year additional imports by considering up to 21 days quarantine period with more flexibility on the turnaround time including vendor's source-based housing in the quarantine. Apart from the above systems, the radioisotope compactor method demonstrated that the solid wastes were able
to compact (1/4 of their original volume) before disposal into the pits **(Figure 6).**

Category	**Potential solutions and Opportunities**
Animal Procurement	Reducing quarantine period based on study duration
	Ethical awareness towards animal use as well as welfare
	Broader range of animal acceptance criteria without compromising science
	Exploring alternate/domestic vendor(s) (e.g., SPF vendor)
	Option(s) of cancelling/deferring animal orders at later stage
Study Design	Establishing and adherence to strict and robust screening triage scheme
	Cassette dosing, analysis and use of rat plasma for calibration curve preparation
	Reducing the control groups and possibility of reusing study and/or unused animals if feasible

	Reducing the number of animals (n) per arm in study groups
	Using less animals for validation and standardization / pilot studies
	Using cross-over study design / Using new/ alternative strain(s)
	Involving veterinary science expertise during species, strain, diet and source selection as well as model development etc.
	Emphasising 3R's principles during protocol review by Institutional Animal Ethics Committee
Alternative methods	Use of simulation and modelling tools
	In-vitro / In-situ / ex-vivo models
	Targeted compound synthesis using CADD and advanced computational biology methods
	Referring to chemotype historical data
	Use of statistical tools (e.g., Bayesian statistics)
	Chemogenomics / population genetics
Metrics	Monitoring of animal procurement and usage of each therapeutic areas
	Calculation metrics and periodical review of the program
Budget	Mandatory budget cut for animal ordering/ Reducing the animal ordering (e.g., up to 15%)
Others	Forum for sharing knowledge, best practices within cross functional team and stakeholders

Table-1 Kaizen event analysis with potential options and possible benefits assessments in vivarium

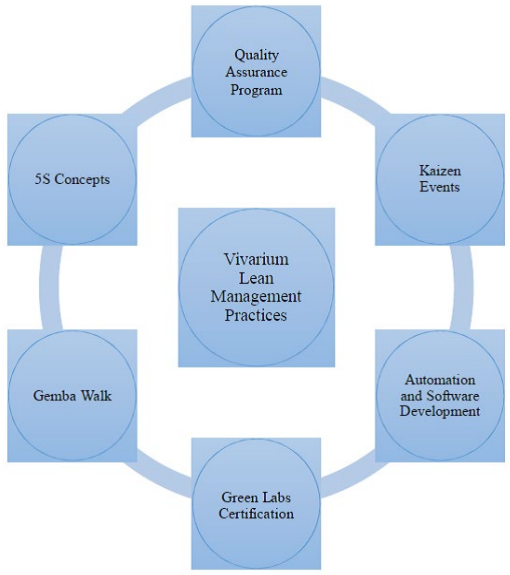

Figure 1: Schematic diagram of vivarium lean management practices and program overview

Figure 2 - Corridor: Unused IVC units parked due to limited space at animal holding rooms which obstructs the movement and obstruct especially during the emergency

Figure 3: Procedure room: Segregated 5S materials occupied work bench and floor space identified as "Red Tag" zone

Figure 4: Clean store: Cage-sets of orderly arrangement on the pallets with labeling for easy tracking of validity period.

Figure 5: Material receipt area: Low-density racks modified and repurposed for consumables along with surplus cage materials arrangement, which improved total capacity vertically as well as and easy access.

Figure 6: Electrically operated compactor used for solid radioisotope materials compaction process with aluminium containers (1/4) prior to the disposal into dedicated pits.

Discussion

Vivarium management requires effective coordination with multiple functions within and/or outside organizations, especially in a collaborative research environment wherein implementation of systems, import of animals from other continents associated with stringent on-site quarantine procedure, investigators support with their scientific protocols and new capability expansions becomes a continuous process. Systematic approach and strategic implementation of lean practices along with monitoring showed better outcomes at workplaces. The lean has been considered a continuous improvement process (Byrne *et al*, 2021), responsible for enabling resources, and infrastructure (Nightingale *et al*, 2002) and noted as strong relationships between lean values and business performance (Bhasin, 2011). Similarly, Lean Construction Maturity Model (LCMM) reported that three key attributes were closely related to the organizational culture i.e., lean leadership, way of thinking, culture and behaviour (Nesensohn *et al,* 2014); which also stated that culture stays based on how an organization performs (Cordes *et al*, 2010). Systematic mapping processes eliminate wastes from the system and full integration maximizes control as well as distribution thereby minimizing the operational resources (Pandey, 2012). The corporate initiatives at our organization explicitly provided several opportunities to think over lean concepts along with cross-functional team members and collective ideas were discussed before the implementation. Brainstorming sessions and subsequent meetings enabled team members to oversee the activities by empowering frontline staff and progress was reviewed at periodical intervals to ensure timelines in order to achieve the targets. During the commencement, capital infrastructure was strengthened over the period to replace low-density racks with high-density options by considering vertical expansion with available space, thereafter, unused racks were parked alongside the corridors and/or buffer animal rooms which became inconvenient to the facility personnel due to frequent movements. A study reported that a team of office of animal care staff developed a kaizen board to indicate the rate of cage change weekly schedule in their work area, identified the wasteful steps then brainstormed and implemented solutions to reduce them,

correspondingly standardizing the process and improving safety (Carbasho, 2013).

At our organization, the kaizen events on 3R's principles provided better results in quarantine, reduction, and refinement of procedures by series of training which was important for scientists (refresher/retraining), organ collection (Lewis, 2000), and other planned surgical procedures were taken care under the approved protocol which further reduced the import of animals. In addition, the kaizen provided several possibilities on study design with rationale for animal reduction while on protocols review and explored the possibilities of alternative methods concerning drug discovery screening tiers wherever appropriate. The animal receipt to experiment completion was monitored by Lab Track software which had given opportunities in terms of colony management, import from multiple vendors traceability, supplies, and timely utilization of animals including protocol notifications contemporaneously to the users. Moreover, the analysis of at least 34 rodent strains imported at various phases for the planned experiments confirmed that around 5% of animals ordered by anticipation of test compounds and able to be utilized for the studies. The kaizen exercise provided flexibility to transfer animals out of specified body weights and/or experimental scope to be transferred under training protocol or other investigators' protocol for the timely usage of animals. A report suggested that the effective application of lean and other quality assurance practices reduced laboratory errors in the areas of molecular biology, microbiology, and pathology (Hollensead *et al,* 2004) and reported significant improvement in patient care in hospitals (Holden, 2011). The quality assurance program monthly compiled observations and subsequent implementation of corrective actions about animal protocol and procedures, facility infrastructure including process improvements transpired measurable outcomes at the workplaces in a systematic manner. Similarly, a study related to animal facilities demonstrated that adopting lean concepts saved energy consumption, capital equipment, space, and innovations in husbandry practices (Stahl, 2013) without compromising animal welfare. Our green lab concept was corroborated with energy savings including the replacement of at least 750 units of compact fluorescent lights (CFL) with light-emitting diodes (LED) fixtures in a phased manner at vivarium and process optimization of cage washers and autoclaved cycles by ensuring least 80% of materials allowed as maximum capacity thereby reduction in the number of cycles, time, and energy conservation. However, a report described that the application of lean principles benefited cage wash areas by reducing time spent on materials identification (Khan *et al*, 2008). Similarly, lean concepts applied by the animal care operations group resulted in the average reduction of process cycle time by 30 minutes and the time saved was utilized for other valuable tasks in the laboratory animal facility (Kovach *et al,* 2019).

The 5S concepts provided opportunities especially housekeeping by identifying the excess inventory was organized under the "Red Tag" category. Our lean efforts substantially reduced wastes in the form of unused materials (non-value-added items) which were segregated (246 items) and approved to transfer to other functional groups to build their additional capabilities as well as academic institutions as part of outreach efforts to support student educational programs thereby freed-up space within the facility. During the mobilization of resources, animal room space was exchanged and allowed further to expand quarantine space in the modified adjacent rooms enabling the additional import of around 25,000 rodents per year by increasing two-fold quarantine holding capacity. Based on the requirements, some of the low-density racks were converted into storage shelves for effective utilization of space and orderly arrangement of consumables including autoclaved materials. The reported outcomes of pathology laboratory lean practices revealed that

the chances of making an error were reduced one by one continuing workflow processes in the cutting and labeling sections to provide timely diagnostic findings more accurately than earlier practices (Cordes *et al,* 2010). Similarly, a case study demonstrated that the lean management approach benefitted for continuous production flow process instead of earlier batch flow as part of control mechanisms (Nenni *et al*, 2014). The development of in-house SCADA software and automation process enhanced engineering controls to perform decontamination (up to 4 cycles per day) with choices of vaporized hydrogen peroxide and chlorine dioxide systems. The enhanced capability was demonstrated to cover the entire facility within the stipulated timeframe based on facility mapping and provided better confidence on decontamination under the barrier conditions. Moreover, a space was identified, and a central diagnostic laboratory was created for pathogens testing as an additional capability to support the health monitoring program. The compilation of refrigerator systems utilization over two years period provided a scope to deploy 40% of the refrigerator units and repurposed them to other functions for effective utilization which further reduced heat load, saved energy, and cleared up space at procedure rooms from various functional areas.

Altogether, the periodical observations and guidance by the veterinary science quality assurance program together with Gemba walk findings greatly helped to understand workplace practices and provided suggestions for improvements to raise the standards of process-related observations along with monitoring oversight by accomplishing the targets through effective coordination. The improved methods of solid radioisotope waste disposal by compaction process reduced 1/4th of its overall volume of waste disposal, allowed ample space, and conserved for future needs especially longer half-life radioactive materials (e.g., ^{14}C and ^{3}H) which in turn preserved the safe work environment within the premises. However, there were challenges initially and learnings while on implementation of new procedures and everyone engaged with continued support during the execution has improved the operational performance by adopting best practices. The entire operational process took profound efforts from cross-functional team members and persistence in the collaborative research environment to improve the quality through lean practices to eliminate waste, reduce time, and energy conservation, optimize space and better ways to reinforce the systems as part of continuous improvements in the workplace.

In conclusion, several lean practices collectively demonstrated measurable outcomes in terms of process improvements on various aspects, effective vivarium management by ensuring the compliance based on periodical observations without compromising animal welfare, increased quarantine holding capacity, energy conservation and systematic implementation of 5S concepts had eventually added value to the systems thereby improved the workplace standards and operational excellence in the laboratory animal facilities.

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Conflicts of interest

The authors declare No conflicts of Interest

Author Contributions The authors contributed at various phases of the 5S implementation and lean management practices including execution in the vivarium.

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