Case Study: **AVEO Oncology**





This is a case study written by Sheryl Perry, MS, LAT, the animal facility manager and IACUC Chair of AVEO Oncology located in Cambridge, MA.

BACKGROUND

AVEO Oncology is founded on a unique drug discovery and development approach known as the Human Response Platform™. This is our way of responding to the needs of the cancer community with integrity, fierce determination and compassion combined with the confidence that we will transform the lives of those impacted by cancer.

This passion is directly related to the operation of the 6,800 square foot animal facility. Consisting of seven animal holding rooms and three procedure rooms, animal models of cancer are created, treated, and studied – all with the intention of translating our findings to associate with those of patients. We have worked with a vast array of cancers, as well as cancer cachexia to broaden the scope of patients we hope to eventually reach.

THE CHALLENGE

In 2011, we began preparing for the relocation of the AVEO Corporate Headquarters to a new 126,000 sq. ft. space located in Kendall Square, Cambridge, MA. It was important to include an evaluation of our animal housing needs and options. As we realized during our investigation, this would play a key role in the design of the new facility.

In our original facility we used standard individually vented cages, which required a dedicated cage-wash infrastructure. Along with two autoclaves, the infrastructure was directly supported by a boiler and individuals who were licensed to operate it. We operated the boiler for 8-12 hours each day.

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Running a vivarium with a cage wash yields extraordinarily high:

- Energy use
- HVAC load (often more than 50% of total HVAC expense of the animal program)
- Steam use
- Service contract costs
- Water consumption
- Detergents
- Labor costs

If we were to install a cage wash in the new ACF, we would also incur high:

- Space per square foot cost
- Construction costs
- Equipment cost

A loss of even one of the autoclaves, cage wash, or boiler has proven to be extremely detrimental to the operation as a whole, not to mention research at AVEO. How would we handle cage processing without them? This led us to search for interim solutions in case we were unable to process cages.

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THE SOLUTION

During the search for a new corporate headquarters, one of the leasing groups introduced disposable caging to our AVEO team. A series of meetings were arranged with Innovive Inc to discuss how they could potentially simplify our vivarium logistics and provide measurable improvement in operative performance. Members of the AVEO community had questions concerning water, environmental impact, recycling, BL2 waste, and overall cost. After this series of meetings with Innovive we understood that by incorporating a disposable caging system, the design of the new ACF now had the potential to be significantly different in size, scope, and cost.





Based on the initial presentation from Innovive, AVEO decided to take part in a three month trial of the Innovive disposable caging system. We ordered one double-sided, 192 cage Innorack®. Other than experiencing the nuances of such a vastly different caging system, one of our goals was to evaluate breeding effectiveness and production. The rack would be reviewed by ACF and research staff, ACF Management, Genetic Models Scientists and the IACUC Chair.

Within the first month, our initial apprehension disappeared with the use of the Innorack® and Innocages®. We incurred a slight increase in breeding production, categorized as 33% over time. After a transition meeting between the AVEO ACF users and our local Innovive representative, we held several internal meetings to discuss the potential option of further incorporating disposable caging. In order to allow more scientists to utilize the new system, a second rack was ordered. The idea of utilizing disposable cages for the facility as a whole was viewed as the wave of the future for the industry.

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Image (left) - 528 cage capacity animal holding room; Image (right) - VHP/sterilization room

The following data was gathered during the meetings with the users of our two Innovive racks:

- Good visibility non-tinted, transparent cage bottom and lid allows immediate visibility to animals, feed, water and bedding
- **Lightweight cages** Each cage weighs only 8.8 ounces and vastly reduces ergonomic risk for animal technicians
- **No bottle dumping** the water bottle lids have screw tops and the lack of a sipper tube allows for the inner pressure to remain stable
- No cage staging or washing allows staff to become more directly involved in the research



- Increased breeding production our data shows an increase of 33%
- More cages per rack size Our largest rack can hold close to 200 cages
- Minimal storage space required we designed a storage room of 155 square feet, which can hold 6000 cage bottoms and a pallet of water
- Increased cage change productivity No unnecessary waiting for items to be washed and autoclaved
- Excellent customer service major advantage in transition process

Our next step was to create a proposal to gain official approval from the IACUC, AV, VP of Research/IO, VP of Finance, and CEO. Shortly thereafter, our transition from a traditional washable caging system to a disposable caging system was approved!



Image (left) - Single main hallway has access to all rooms; Image (right) – 544 cage capacity animal holding room, Innocart™ transportation cart at the bottom right

THE RESULTS

Waste Processing

Innovive provides their customers with a closed loop recycling process for all cages and accessories. Once 1,600 cage bottoms are collected, Innovive will transport them to one of their two recycling facility for recycling and composting.

The majority of AVEO's In-vivo work is BL2, which is non-recyclable. We wanted to be a part of the process in being as green as we could. After working with a number of waste removal companies, we spoke with the Managing Director of Triumvirate Environmental. We now treat all of our cage bottoms as BL2, and they are sent to a Waste to Energy



plant. On average we create 11 boxes of BL2 waste per week, approximately 1,000 cages.

In order to stream-line our non-BL2 Innovive waste and accommodate the square footage needed by researchers, we contracted with Re-Stream, a local waste removal company to remove the recyclable products. Each animal holding room has a 64-gallon rolling tote that all cage lids, feeders, water bottles, cage card holders, and accessories are placed into. These are replaced on an add-needed basis.

Transition and Design

Due to internal issues at AVEO, it became necessary to move the research labs and ACF to a temporary space prior to the opening of the Corporate Headquarters. The AVEO Executive Team performed walk-throughs of available buildings in the area, and settled on a space that had ample square footage for the research labs and an accompanying small ACF. With the addition of Innovive, the necessity of finding a location with an operating cage wash was not needed. This move to the temporary facility gave ACF Management, staff, and users the opportunity to perfect the use of the new caging system prior to the second and final move. It also allowed us to prepare for the new facility and made the transition to the newly designed ACF very smooth.

With the utilization of Innovive Disposable Caging, the design of the new ACF was very user friendly. The caging system occupied a smaller footprint which allowed us to not only create a larger research lab, but additional holding and procedure rooms. Not having to dedicate space for cage processing provided us with the ability to create a transfer room, with ample space for incoming packages and storage for waste inside the facility. A room that housed a VHP generator, complete with the capability of full exhaust, was designed to sterilize mouse racks.

Cost

Economics and value proposition were important for AVEO during the decision making process. There are two primary categories of cost associated with animal facilities:

- 1) Capital equipment and infrastructure costs
 - CapEx utilization and low starting costs
 - Racks and caging
 - · Washers and sterilizers
 - Square footage
 - Design, project management, and construction fees
- 2) Ongoing maintenance and operation expenses
 - Labor (washroom and staging technicians)
 - Utilities
 - Maintenance and supplies
 - Service contracts
 - Management time

As you can see from the data listed in the chart on the next page, a substantial amount of cost and physical space is tied to supporting the cage washing process, which means it would be diverted from space and finances that would directly contribute to furthering research and science. We tracked the finances for one year of the upkeep and maintenance of the boiler, cage wash and autoclaves. We spent approximately \$240,000 per year. This includes two FTE's that would not be needed with a disposable cage facility.

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After examining the cost of ownership and maintenance of both washable and disposable cages over the course of 10 years, we calculated a savings of \$2,211,440 (45%) by using the Innovive disposable caging system. One of the factors that brought this to light, was the initial savings on build-out of an animal facility without a cage wash infrastructure.

Image (below) - Cost comparison between traditional and disposable caging

1. SIZE OF FACILITY	Mice	Rats
Number of cages	3,000	-
Average capacity	75%	0%

2. TRADITIONAL CAGING ASSUMPTIONS		
Rack capacity	160	60
Cost per rack (including cages)	\$25,000	\$0
Cost of replacement cages	\$50	\$100
Buffer supply of cages to support wash cycle	25%	25%
Average cage lifetime (years)	3.0	3.0
Annual cage breakage	2%	29
Cage change interval	14.0	7.0
Labor: Cages changed per person per day	200	125
Labor: Fully loaded cost of technician	\$ 65,000	\$ 65,000
Total racks required	19	-
Buffer cages required	750	-
Total cages required	3,750	-
Cage changes per year	58,661	-
Annual cage replacements	1,250	-
Annual cage breakage	75	-

 60
 Build out and construction of washroom
 \$ 700,000

 \$0
 Capital equipment - Washers
 \$ 250,000

 \$100
 Capital equipment - Sterilizers
 \$ 80,000

 25%
 Capital equipment - Bedding delivery
 \$

 3.0
 Capital equipment - Robotic, other
 \$

 2%
 Annual washroom maintenance/supplies
 \$ 22,500 kr

 7.0
 Annual washroom tullities
 \$ 30,000 E

 125
 Labor: Number of washroom staff
 2.00

 15,000
 Labor: Fully loaded cost of employee
 \$ 65,000

Project-specific costs to build infrastructure. Set to zero only if there are no construction, renovations or equipment required

Include equipment service agreements, travel/parts, chemicals, mops, boots Excludes washroom HVAC

NOTES: Traditional section:

3. INCREMENTAL WASHROOM AND OTHER COSTS

Excludes value of increased capacity (or recaptured space)

Excludes value of management time redirected to science

Excludes reduced cost of grievances, absenteeism and overtime of cage wash activities Excludes value of reduced risk due to simplified process and significantly fewer cage changes Excludes value of increased scientific and operational flexibility as the program changes over time

4. DISPOSABLE CAGING ASSUMPTIONS		
Rack capacity	176	80
Cost per rack	\$12,535	\$14,720
Cost per Innocage change	\$2.76	\$5.59
Cage change interval	14	10
Change out efficiency gain	15%	15%
Labor: Cages changed per person per day	230	144
Labor: Fully loaded cost of technician	\$ 65,000	\$ 65,000
Total racks required	18	-
Cage changes per year	58,661	-

NOTES: Innovive section:

Rack pricing estimated; includes volume discounts

Cage pricing makes assumptions about lid and feeder reuse through multiple cage changes 14 day cage change assumption can be higher with fewer than 5 mice per cage

Annual inflation 2.5%

5. TRADITIONAL CAGING EXPENDITURES										
	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10
Equipment:										
Cost of racks	\$475,000	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Cost of additional cages	\$37,500	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Annual cage replacement cost	\$46,875	\$48,047	\$49,248	\$50,479	\$51,741	\$53,035	\$54,361	\$55,720	\$57,113	\$58,540
Annual cage breakage cost	\$2,813	\$2,883	\$2,955	\$3,029	\$3,104	\$3,182	\$3,262	\$3,343	\$3,427	\$3,512
Total rack and cage cost	\$562,188	\$50,930	\$52,203	\$53,508	\$54,846	\$56,217	\$57,622	\$59,063	\$60,539	\$62,053
Washroom:										
Washroom build out and equipment	\$1,030,000	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Lost revenue and/or time during renovation										
Washroom maintenance and supplies	\$22,500	\$23,063	\$23,639	\$24,230	\$24,836	\$25,457	\$26,093	\$26,745	\$27,414	\$28,099
Annual washroom utilities	\$30,000	\$30,750	\$31,519	\$32,307	\$33,114	\$33,942	\$34,791	\$35,661	\$36,552	\$37,466
Total washroom cost	\$1,082,500	\$53,813	\$55,158	\$56,537	\$57,950	\$59,399	\$60,884	\$62,406	\$63,966	\$65,565
Labor:										
Vivarium technicians	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1	1.1
Washroom labor	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Total labor costs	\$203,326	\$208,409	\$213,619	\$218,960	\$224,434	\$230,045	\$235,796	\$241,691	\$247,733	\$253,926
Annual costs	\$1,848,013	\$313,151	\$320,980	\$329,005	\$337,230	\$345,660	\$354,302	\$363,159	\$372,238	\$381,544
Total cost	\$	4,965,283								

6. DISPOSABLE CAGING EXPENDITURES										
	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10
Equipment										
Cost of racks	\$225,630	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
Annual cage costs	\$161,904	\$165,951	\$170,100	\$174,352	\$178,711	\$183,179	\$187,759	\$192,452	\$197,264	\$202,195
Total rack and cage cost	\$387,534	\$165,951	\$170,100	\$174,352	\$178,711	\$183,179	\$187,759	\$192,452	\$197,264	\$202,195
Labor:										
Vivarium technicians	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Labor costs	\$63,762	\$65,356	\$66,990	\$68,664	\$70,381	\$72,140	\$73,944	\$75,793	\$77,687	\$79,630
Total costs	\$451,295	\$231,307	\$237,090	\$243,017	\$249,092	\$255,319	\$261,702	\$268,245	\$274,951	\$281,825
Total cost	:	\$ 2,753,844								

Total savings \$ 2,211,440

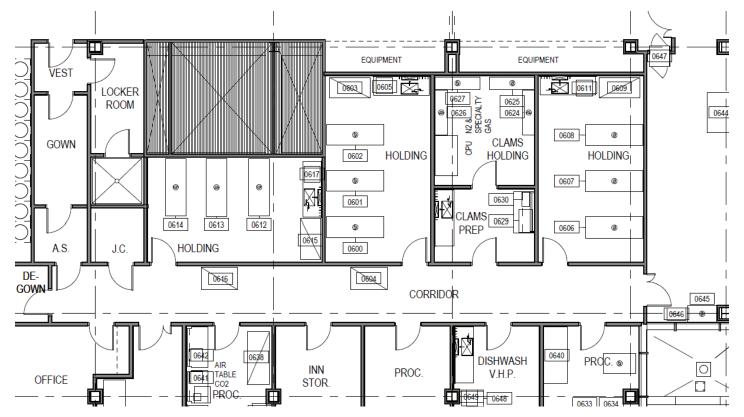


Image (above) - AVEO Oncology floor plan without a cage wash

Conclusion

The investigation of and transition to Innovive Disposable Caging for AVEO Oncology played a large role to the success of the new corporate headquarters. Cost savings incurred, management improvements, changes in staffing responsibilities were all considered throughout the investigation. Improvements in technology of equipment and to the industry as a whole was the icing on the cake.

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