

## **Support for Living Stock Collections: A Mammalian Stock Center Perspective**

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**Key words:** Peromyscus, financial support, living stocks, funding

**Funding:** The PGSC is supported by a grant from NSF (Award Number: 1755670).

**Disclosure statement:** The author has nothing to disclose

*The living stock collections represent an indispensable resource for the life scientists. Their uninterrupted operation should combine high quality standards, cost-effectiveness, wide accessibility and sustainability. Mammalian stock collections, especially those involving diversified animals, face some unique challenges that may disrupt their smooth operation if not addressed.*

Living stock collections maintain wild type or mutant stocks of various species and distribute them to the investigators that are requesting them (1). They also function as central repositories that can receive, preserve and re-distribute specific stocks that are considered of special interest to the scientific community (1). Finally, they operate as clearinghouses accumulating and disseminating information relevant to the organisms that are supported (1). Their continuous operation warrants the availability of the stocks maintained in a timely manner, rendering these experimental tools readily accessible to all interested investigators for a small fee that may cover a fraction of the operational cost. The user fees usually supplement the funds provided by the major central government agencies that support scientific research, such as the National Science Foundation or the National Institutes of Health. Usually, an “on demand” expansion or reduction of the individual stocks that are maintained in captivity, absorbs the fluctuating external demands and warrants the financial sustainability of the stock centers, without compromising the desired and mandated quality standards.

If, how and at which extent the living stock collections should be supported by the central funding agencies are topics of ongoing debates. The National Science Foundation stopped in 2016, for about a year, to provide support for the Collections in Support of Biological Research, in an attempt to re-adjust existing priorities and align them to the current needs (2). More

recently these concerns were epitomized in a recent call of the National Academies of Sciences, Engineering, and Medicine, at the request of the National Science Foundation, on *Biological Collections: Their Past, Present, and Future Contributions and Options to Maintaining Them* (3).

Over the last few years during which the living stock collections increased in number and usage, two diverged models predominated regarding the mode of support of the stock centers: According to the first model the centers should be supported by funding from central agencies which in turn provided the stocks to the users for a minimal only fee. According to the second model the centers' operation should be supported exclusively by the user fees in a manner according to which funding agencies provide appropriate funds to the grant recipients that in turn purchase the stocks from the stock centers. Obviously, in the former model the cost of the animals is minimal because it is offset by funds offered directly to the centers while in the latter it is increased because the centers' operation relies exclusively on the usage fees. Hybrid models also emerged at which the balance was shifted towards each direction pending the availability of funds.

The operational model at which the supply and the demand are dynamically adjusted over time is readily applicable when the stocks that are distributed can be cryopreserved and are also genetically identical or well defined. This way, requests for the same stocks or strains, even though they occurred at different times, result in the supply – to a feasible extent - of identical animals. A typical example for this category is the conventional laboratory mouse for which the availability of advanced rederivation methodologies, in combination with the inbred nature of the experimental mice renders the “on demand” supply feasible due to the rapid expansion per request of individual animals. When however, the stocks that are being maintained are

genetically diverse, or if well optimized cryopreservation and rederivation technologies are not yet available, the options for the sustainable operation of the corresponding centers are limited, facing some unique challenges.

The model at which the operational costs are directly passed to the users appears more efficient businesswise and rational as compared to the model at which the centers are supported centrally, directly by the funding agencies. It suffers though from major inherent limitations that may compromise the value of the living stock collections as providers of stocks to the scientific community in an uninterrupted and continuous basis. In such business-efficient model at which the living stock centers must be self-sustained, in order to remain viable, they are required to reduce their operational costs and therefore the supply should always remain moderately lower than the demand, so the production of animals that will remain unutilized and will eventually cause financial losses will be eliminated or minimized. Demand however does not remain stable over time. Changes in research priorities and the availability of research funds are unavoidably reflected to the demand for specific stocks, which however, despite the transiently reduced utilization should be maintained at levels above certain thresholds to avoid loss of genetic diversity. It could be argued that a logistically rational solution for this issue would be to apply higher user fees for the “rare” or underutilized stocks in order to compensate for the losses that may have incurred at periods of lower demand. This is indeed a sound strategy which however is applicable only up to the point that the new, higher user fees are still below the cost of animals that can be maintained in other than the stock centers’ facilities. If they exceed these costs, peripheral colonies will be unavoidably established at which the cost for the maintenance of the corresponding stocks can be lower than that of purchasing the animals directly from the stock center and that eventually may even partially substitute the living stock centers as suppliers of

animas to the scientific community. Indeed, this is common for laboratories that use specific stocks on a rather continuous basis. Yet, such peripheral colonies will not have to satisfy the rigorous quality standards that the stock centers are bound to adhere as part of their regular operation. Furthermore, accessibility of the stocks to outside investigator will remain “at the will” of the investigators that are maintaining them. Implications of such developments are foreseen at both a purely scientific level and even beyond that.

Unavoidable bottleneck effects will cause the establishment, expansion and eventually distribution of stocks that may be genetically distinct from those originally obtained by the stock centers. This will have profound implications in the quality of the results that will be generated by investigators that practically will be using stocks different from those originally described, challenging increasing concerns on rigor and reproducibility of scientific research (4,5). In addition, since animals will not be maintained at numbers sufficient to satisfy outside requests, the availability of stocks to external investigators may also be impeded, as it will rely exclusively on the surplus of animals in the existing outside colonies. The latter will eventually obstruct the accessibility of the stocks to the scientific community.

These are all concerns that have to be taken into consideration when the mode of the Stock centers’ support is decided and suggest that models relying primarily on utilization should not be the choice for their support.

### **Acknowledgement**

The *Peromyscus* Genetic Stock Center is supported by a grant from NSF (Award Number: 1755670).

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