Scale up considerations for NAMs

Cuanalo-Contreras, Karina · Monteban, Vivian · Benkmann, Dennis
SABEU GmbH & Co. KG · Detlev-Karsten-Rohwedder-Str. 10 · 37154 Northeim · Germany
karina.cuanalo@sabeu.com, vivian.monteban@sabeu.com, dennis.benkmann@sabeu.com

SABEU PLASTICS & MEMBRANE TECHNOLOGY

Introduction

For many years *in vivo* testing has been the gold standard for toxicology. Currently, the field is transitioning towards the use of new approach methodologies (NAMs). In this regard, the supplier industry has been diligent in the fostering of NAMs and there are many cases of synergy with other stakeholders towards the 3Rs principle. Despite these advances, the wide adoption of alternative *in vitro* methods is a current challenge. From our 60-years of experience as plastic and membrane OEM of commercial off-the-shelf and customized NAMs, we would like to summarize the fundamental points to translate ideas in line with financial and regulatory specifications.

In vivo to *in vitro*

In the last decade the use of animals for scientific purposes has been largely reduced. Scientific breakthroughs and regulatory paradigm shifts are key ingredients in this transition. Currently, there are 49 NAMs included in OECD test guidelines. In addition, *in vitro* testing for skin sensitization and eye irritation has been made default by REACH EU and for about a decade, cosmetic testing in animals is banned in several regions. More recently, The European Parliament voted to phase out the use of animals in research, testing and education. This is an important step aiming to accelerate the *in vivo* to *in vitro* transition and a recognition on the potential of NAMs.

Scale up considerations

The industrial production of an *in vitro* NAM demands communication, time and resources. From the very beginning, we advise to think on the functional and non-functional requirements of the initial industrial prototype. By doing this, unnecessary project iterations can be prevented.

For a proper industrial NAM design, the following points should be considered:

(a) Material selection and tolerance levels to comply with biological evaluation according to applicable standards

(b) Regulatory strategy and standards

(c) Environmental conditions, packaging, labelling and transport profile

(d) All critical quality parameters affecting homogeneity of cell growth to enable reproducible results

(e) Quality control and product acceptance levels

(f) Objective measures to prove successful verification of requirements

(g) A well-balanced interaction of ergonomics, appearance, functionality, technology, and ecology

To ensure the highest quality of a NAM device at larger volumes, it is important to select an industrial partner with a strong reputation for each of the single components and their assembly into a final product.

For NAM devices composed by a plastic support and a semipermeable membrane, special considerations must be taken into account. Namely, each section of the semiporous membrane – that serves as support for cell growth – must have the same pore size distribution. In addition, the membrane must be appropriately coated and evenly welded to the plastic. If any single element is defective, the whole cell culture will be damaged. Consequently, those aspects are crucial. An example of such device can be found in Figure 1.

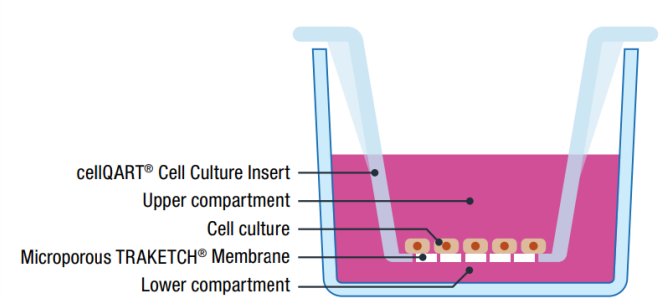

Figure 1. *Schematic representation of a cell culture insert composed of a plastic support and a semipermeable membrane.*

Conclusion

The supplier industry has been actively involved in the promotion of the use of NAMs and there are many positive examples of cooperation between manufacturers and scientists towards the development and implementation of new *in vitro* methods.

The effective industrial manufacturing of NAMs is critical to accelerate the *in vivo* to *in vitro* transition. To efficiently translate a NAM into regulatory, commercial, and technical requirements for large-scale manufacturing, the early engagement with a mature industrial partner is encouraged.

As original manufacturer, we are actively looking for opportunities, collaborations and projects that can benefit from our expertise on the production of cell culture microporous membranes, plastics and cell culture inserts.