



Engineering Regenerative Medicine's Future

Global Standards in Conjunction with Enabling Technologies Hold Key to Advancing the Field

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Stakeholders in the regenerative medicine sector recognize that the commercialization of novel therapeutic interventions faces a number of bottlenecks before these treatments can be adopted by existing healthcare providers. Since companies focused on regenerative medicine first attracted investment, many firms have identified opportunities and have set about attempting to commercialize them.

However, only a handful of companies have actually been able to solve the technical and commercial challenges and reap the rewards. While proof of therapeutic principle may be established early in the development process, many of the product development and manufacturing challenges that lie in wait to kill off a concept could be avoided if the engineering challenges are addressed in parallel.

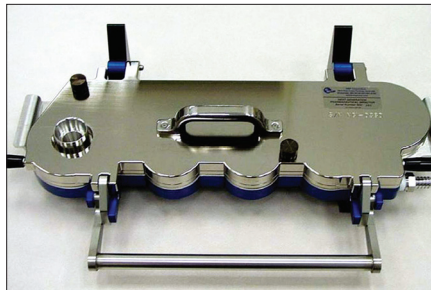
There are a number of key issues that need to be addressed by the regenerative medicine industry collectively in order for product-development activities to generate significant levels of investment, and to see products being taken up by healthcare systems in volume.

From an engineering and product development perspective, two critical issues need to be resolved in order for the vari-

ous resulting therapies to go mainstream: development and implementation of standards, and reducing the cost of goods. In both cases it is clear that overcoming many of the major barriers for those at the cutting edge of regenerative technology lies in precompetitive collaboration. In this article we've focused on the requirement for standards.

Standards

Regulatory guidance covering the development of regenerative medicine therapies exists; however, there is room for considerable subjectivity in the interpretation of these guidelines by sector stakeholders across different territories. The value of developing and introducing formal standards across common research, development, and production processes is that it provides a basis for best practice,



The Next Generation Impactor, developed by a pharmaceutical industry consortium, was invented to overcome the low productivity issues inherent with the Andersen Cascade Impactor.

and thus aligns and potentially expedites commercialization of therapies.

As a guiding principle, the formalization of best practice into recognized standards should be a constructive process for the benefit of the industry as a whole. That is to say, it is not so much about restrictive rules; it is about the development of common, validated methods and solutions that contribute to quality, safety, and performance.



Widely used since the 1950s, the Andersen Cascade Impactor was, until recently, the gold standard for measuring particle size distribution from inhaled drugs or an air sample.

By working within a common standards framework, companies operating in the regenerative medicine space can share best practices and use this as a platform upon which to accelerate innovation. There is also opportunity to position these standards as a benchmark upon which regenerative medicine therapies, and the underlying processes by which they are derived, must meet to gain regulatory approval.

The field of regenerative medicine is a complex regulatory environment, heavily segmented with many different variants and definitions of what constitutes regenerative medicine. It is also a multidisciplinary field covering, for example, tissue sampling, manipulation of cell lines, encapsulation, information handling, and delivery devices.

As with many other sectors before it, validated methodologies are being created internationally, and so standards need to be harmonized globally. A wider challenge that emerges once a standard or best practice has been agreed upon by stakeholders is how to achieve widespread adoption.

Developers of regenerative medicine need to be able to demonstrate cost-effective, expedient development programs combined with feasible commercialization strategies in order to attract significant investor funding. Equally, robust exit strategies for investors also need to be defined in order to attract funding in the long term. The introduction of harmonized standards as a means to de-risk generic R&D and production processes can support these commercial considerations.

A Need for Enabling Technologies

Facilitating these standards will require the design and engineering of robust enabling technologies to address development and manufacturing chal-

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lenges, and demonstrate product safety and/or efficacy.

These should be easy to use and provide reproducible results across multiple locations and usage environments, despite variation in user input. This approach also envisages the repositioning of existing platform technologies that are currently utilized outside the regenerative medicine field.

Take a specific example: the EC published Directive 2004/23/EC concerning standards of quality and safety for the donation, procurement, testing, processing, preservation, storage, and distribution of human tissues and cells. Article 23 of this directive requires establishments involved in distribution to comply with specific requirements to ensure the quality of tissues and cells during transit.

Here is an opportunity to develop enabling technologies that ensure that the environmental conditions in which tissues and cells are kept are within acceptable quality levels through the workflow. Furthermore, they should ensure that full recording of relevant conditions, such as temperature and physical shock, can be made.

Other common challenges pursuant to this sector, which may lend themselves to standardized approaches, include the following:

- bioprocessing, particularly manufacturing controls and metrology, including systems for batch release inspection and data logging; and
- physical delivery of the therapeutic into the subject—common or modular device platforms optimized to avoid cellular damage (through shearing forces) and capable of dealing with small delivery volumes.

In many cases the development of enabling technologies might most effectively be undertaken on a precompetitive footing in order to address generic processes faced by the industry as a whole.

To illustrate this point, consider an enabling technology widely used in respiratory pharmaceutical development.

The Andersen Cascade Impactor (ACI) was developed for the size resolution of aerosolized particles, such as dry powder formulations intended for use in inhaled devices.

The ACI has been instrumental in standardizing a key aspect of regulatory development of inhaled medicines. The first generation of impactors required a labor-intensive protocol, which did not lend them to high-throughput analyses. Furthermore, the device was difficult to clean following each analysis.

To attempt to resolve these issues, a 15-member pharmaceutical industry consortium developed the Next-Generation Impactor (NGI). Substantial user involvement in the design process resulted in an easier to use, higher-performance, precision cascade impactor for testing metered-dose, dry-powder, and similar inhaler devices.

In this case, it was only when parties with a common interest got together on a collaborative footing to pool technical and commercial resources that the design for the NGI became more fit for purpose, rather than attempting to utilize nondedicated instrumentation for suboptimal development activities.

The example shows how collaborative development promises to support the industry as a whole where the players face specific challenges that are generic to the field and that the industry cannot afford to overlook in its pursuit of overcoming developmental or production bottlenecks.

As demonstrated in the examples in this article, the development of these enabling technologies is often best approached proactively through precompetitive collaboration. And, just as standards need to be harmonized globally, so too does the collaboration.

We believe that it is through the development and adoption of these harmonized and global standards, as well as the reduction of the cost of goods, that engineering and product development will be able to support the regenerative medicine industry finally going mainstream. **GEN**