A view into the challenges and contributions of GMP facilities

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Challenges of running a GMP facility for regenerative medicine in a public hospital
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The field of regenerative medicine is researching and developing numerous cell-based therapies to address many different medical conditions. In Europe, approved 'Good Manufacturing Practice' (GMP) facilities are required to produce cells used in these cell-based treatments to ensure safety and meet quality standards. Dr Mariele Viganò and her colleagues describe the challenges of establishing, maintaining and meeting compliance with EU standards for a GMP facility as well as offer insight to how public GMP facilities contribute to developing future regenerative medicines.

What questions & challenges are raised?

Research in the field of regenerative medicine is leading to new clinical therapies that repair or replace damaged cells in tissues and organs. Many of these treatments use various types of cells, including stem cells or immune cells, which are often grown or manipulated in a laboratory. The European Union has specific regulations that designate cell-based therapies used for treatments as 'Advanced Therapy Medicinal Products' (ATMP). The EU regulations also specify that biological materials used for AMTP must be handled in facilities that meet standards of 'Good Manufacturing Practices' (GMP). These standards are the same as what pharmaceutical drugs must meet for production and quality control, but also require stringent microbiology conditions for growing cells for human use. Dr Mariele Viganò and her colleagues from the Ospedale Maggiore Policlinico in Milano describe in a special report the requirements and multiple challenges they faced in the process of establishing and maintaining a new GMP compliant cell manufacturing facility in a public hospital. The authors offer suggestions for others establishing GMP facilities and highlight the importance of participation from patients, academia, industry and clinics.

What insight & direction does this give for research policies?

The GMP facility that Dr Viganò and her colleagues work at is part of a public hospital, but financial support for building and maintaining the facility has largely come from private donations and a business model focused on being an academically oriented research and manufacturing center. This means the facility helps translate academic research into clinical GMP procedures and products for clinical trials. The authors note there are many different business strategies a GMP facility might adopt, but academically oriented facilities should carefully consider their objectives and risks when undertaking scientific research, developing initial AMTP manufacturing processes to hand off to industry, and fostering academic initiatives to 'spin-off' as independent businesses. Another important consideration is the role and support of patients and their organisations, who participate in trials, contribute to data collection, supply precious samples and act as fundraisers. Industry also plays a significant role in the development of ATMP, often partnering with academics to work synergistically together. Phase I and II clinical trials are primarily based on research and support from academic institutes, whereas companies offer expertise in developing therapies for later stages, phase III clinical studies and market authorisation. The authors note the interplay of patients, academic institutes and industry situates many public GMP facilities in a position between care, research and industry. This in-between status can put public GMP facilities in 'limbo' for funding, relying on an assortment of funding opportunities and without any form of stable funding. The authors close by stating that building strong networks and partnerships between patient organisations, public and private institutions, regulatory agencies and industry will be key to successfully deliver therapies to those that currently have no options.

What background and point are discussed?

The initiative by Ospedale Maggiore Policlinico to develop a GMP facility for ATMP production was started in 2000 and received GMP certification in 2007. Dr Viganò and her colleagues note that their center was purpose-built to meet GMP requirements for controlled environments. The building's layout aims to maximise efficiency by considering the workflow of all 'life-stages' of production, manufacturing and quality control. The GMP staff of the Ospedale Maggiore Policlinico have advanced degrees in biology or medicine, yet most still required additional training to 'transform' them into pharmaceutical production and quality control specialists. The authors state that the center focuses primarily on developing AMTP addressing unmet clinical needs, supporting phase I, II and III clinical trials and undertaking research to better understand the biology of cell-based therapies. In their discussion about creating and maintaining a GMP facility, Dr Viganò and her colleagues note that quality assurance of the biological products being manufactured raised several issues. Quality assurance staff in hospitals typically focus on ensuring good patient care rather than evaluating if biological products meet pre-defined characteristics. Thus, training hospital quality assurance staff to understand these differences was important and was greatly helped by the cooperation of cell manufacturing staff. GMP facility guidelines require that an "adequate number" of appropriately trained personnel must be employed to cover specific responsibilities and meet production demands. The authors note that finding personnel with experience and specific qualifications was difficult, particularly for cell manufacturing staff with pharmaceutical production training and hospital quality assurance staff qualified to monitor cell-therapy quality control. Production of AMTP in a GMP facility requires that living material and cells must be processed and handled in extremely clean environments, where air quality and equipment cleanliness are continuously monitored. This involves multiple staff dressing rooms with increasing air cleanliness and special ventilation pass-boxes for equipment to transfer in and out of these areas. Finding staff capable of installing, operating, maintaining, and repairing clean-room equipment to meet GMP requirements was challenging and sometimes required service contracts with external companies. The authors note that GMP standards for documentation have required considerable resources to record, monitor and control the numerous details of ATMP production. Integrating these details into hospital data systems also presented difficulties. Production and quality control of AMTP also required addressing several challenges caused by the inherent variability and instability of living cells. The authors remark that risk assessment strategies are very valuable for driving and supporting decisions regarding challenges and other issues their facility encounters.