and musculoskeletal diseases. Additional EU and Canadian GCTs target congenital and immunologic disorders, whereas US products include a cosmetic and periodontal GCT. Three GCTs were based on allogeneic starting material. Concerning evidence, significant results on the primary efficacy endpoints were provided for a large proportion of approvals (10/14). Less than half of approvals involved orphan drugs (EU = 4, US = 1). Orphan drugs in the EU were often approved under alternative (e.g. conditional approval) pathways (3/4), enabling single arm trial design and non-significant results on clinical endpoints. On the contrary, approvals under US (4/5) and Canadian (1/1) alternative (e.g. US accelerated approval) pathways are predominantly based on randomized, controlled, phase III trial design (US, Canada) and significant results on clinical endpoints (US). Unmet medical need is often considered together with safety and efficacy uncertainties in decision-making for approval in the EU (5/8; US 2/5; CA 1/1). In conclusion, product profiles differ between jurisdictions, which influences scientific evidence and regulatory assessment criteria to gain GCT approval. More orphan drug designation in the EU results in approval under alternative pathways based on less robust clinical trial design and efficacy evidence compared to the US.

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DECISION-MAKING ON MARKETING AUTHORIZATION OF ADVANCED THERAPY MEDICINAL PRODUCTS IN THE EUROPEAN UNION

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Introduction: Advanced Therapy Medicinal Products (ATMPs) are innovative products receiving increasing interest. While many clinical trials with GCTs have been performed in Europe, currently only fifteen marketing authorization (MA) applications have been submitted (December 2016), which resulted in eight MAs. This study aims to investigate how decision-making and the underlying evidence for (non-)MA is built up in the EU.
Methodology: A comparative analysis was used to investigate the justification of MA-decision procedures of ATMPs. This was subcategorized and scored into product profiles, scientific evidence and regulatory assessment criteria. How these factors relate to each other is compared between MAs and non-MAs.
Preliminary Results: Eight applications were granted approval, including standard MA (n = 5) and alternative MA (n = 3). Six applications were not granted approval (non-MA). Clinical trial design differed between standard and alternative MA, whereas the clinical trial designs of the non-approved products showed high variability. Alternative MA (n = 3) trials included less patients (mean alternative MA = 57 vs. mean standard MA = 244) and randomized controlled phase III trials were not conducted. Furthermore, these alternative MAs were all designated as orphan drugs, for which alternative treatment was lacking, and the products showed added clinical benefit. Moreover, considerations of unmet medical need were part of decision-making for these alternative MA products. For standard MA, decision was always based on statistical significant results on the primary efficacy endpoints, whereas such results were not always obtained for alternative MAs. Moreover, for the non-MA products statistical significant efficacy on primary and secondary endpoints were lacking.
Conclusion: This study suggests that key assessment criteria in approval of ATMPs in the EU are trial design, significant outcomes, orphan designation and unmet medical need. In particular, ATMPs developed for orphan indications generally enter alternative regulatory pathways, which influences clinical trial design, clinical outcomes and the weight of unmet medical need in decision-making for ATMP approval.

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IMPLEMENTATION OF A PROGRAM FOR THE EXTERNAL AUDIT OF CONTRACTED SUPPLIERS BY AUSCORD—THE AUSTRALIAN PUBLIC CORD BLOOD COLLECTION AND BANKING NETWORK

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Contracted suppliers of critical materials, reagents, services and equipment must be audited and qualified to verify compliance with written agreements and relevant standards. External audits may be challenging for cellular therapy facilities faced with large numbers of contracted suppliers and often limited resources. As part of an operational alignment project, AusCord created a system to integrate and coordinate the audit of external suppliers. A master register was established and included a list of suppliers and services provided, a uniform process for risk assessment and an audit schedule. A procedure and forms were developed to manage the process. Each cord blood bank (CBB) registered their suppliers to identify common contractors and performed risk assessment of individual suppliers. Results were compared between the three CBBs to develop consensus on a single scale and risk rating matrix. Each supplier was then rated based on the degree of regulatory oversight, criticality of their service and the presence of prior non-conformances. The level of risk was used to determine whether an audit was required and if so the type of audit to be performed (on-site audit, desk-top audit or a questionnaire). Audits were allocated to each CBB and scheduled. A total of 27 audits were allocated in the first year. The results of completed audits are reviewed at face to face AusCord meetings. To date we have had 100% compliance with respect to supplier cooperation. Audit outcome will be used to determine the frequency and type of subsequent audits for individual suppliers. The AusCord coordinated system has provided significant benefits to the various stakeholders. The use of a standardized integrated approach to risk assessment and audit of suppliers and the consolidation of audits has resulted in increased surveillance of suppliers, improved supplier response rate, CBB access to a more comprehensive and concise summary of supplier performance and effective and efficient utilization of resources.

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PROCESS MAPPING, DOCUMENT TEMPLATES, AND DASHBOARDS TO SUPPORT CONSISTENT, THOROUGH AND RAPID OF EARLY PHASE INDS

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The Human Cell Therapy Lab at Mayo Clinic in Rochester, Minnesota is a cGMP facility focused on bringing new cell therapies to difficult to treat diseases. The early history of the lab was focused on developing and validating platform cell technologies in preparation for clinical use. As the lab moved these technologies toward the clinic, it became clear that physicians had limited experience in the processes or regulatory submissions. As the common denominator in all of the trials, the HCTL became the de facto expert in regulatory submissions. We found ourselves repeating many aspects of the process as new protocols utilizing HCTLs platform technologies came on line. To accelerate IND construction, and to produce a uniform package for FDA review, we process mapped the decision tree and construction of the IND. We templated all required documents, provided examples of completed documents, and developed a dashboard to assign tasks and monitor completion. The combination of process mapping, consultation, written examples, and project management has led to a dramatic improvement in the efficiency of regulatory submissions. We believe it has also improved the uniformity of submissions to the FDA. In all, we have used this process to obtain approval for more than 23 protocols, representing more than 15 INDs that have now been used to manufacturing more than 300 products for patients under IND. We believe that the elements of this process can be implemented in other academic medical centers to centralize, optimize and streamline the process of regulatory IND submissions. We will present these elements, and describe the best practices for their use.

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ACCELERATING T CELL PRODUCT DEVELOPMENT: TRANSITIONING FROM THE LABORATORY TO THE MARKET

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Objective: 1. Define appropriate methods to accelerate T cell product development based on the product and the patient population. 2. Identify regulatory