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Securing raw materials, reagents, and consumable supplies in the academic bioproduction UNITC network: because the chain is only as strong as its weakest link

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Academic autologous cell manufacturing offers key advantages, including cost-effectiveness, accessibility, and flexibility. However, the management of Raw Materials, Reagents, and Consumables (RMRCs) is essential for ensuring product purity, safety, and effectiveness. Variations in RMRC quality can increase production costs and result in batch failures. This work from the GMP-Bioproduction group of the French Consortium in Advancing Cancer Cell and Gene Therapy (UNITC) outlines a multicenter study conducted from 2022 to 2024 across all 11 French academic cell and gene therapy facilities producing Advanced Therapy Medicinal Products, evaluating current RMRC management practices. The study highlights significant challenges, including supply shortages, reference changes, and inconsistent quality controls. While RMRC-related non-conformities accounted for only 6.8% of total issues, they frequently required complex procedural adjustments, resulting in added financial and operational burdens. Despite differences in production scale and ATMP types, all centers consistently evaluated the criticality of RMRC, reflecting strong alignment in risk assessment practices. To address these issues, the study proposes recommendations, including a unified RMRC risk classification system, harmonized quality assurance processes. These actions aim to strengthen regulatory compliance, enhance collaboration across academic centers, and improve the overall resilience of academic decentralized CAR-T cells manufacturing in France.

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INTRODUCTION

The bioproduction group of the French Consortium advancing Cancer Cell and Gene Therapy (UNITC) is a national consortium focused on research in Cell and Gene Therapies (CGT), established in late 2023. It brings together leading experts in academic manufacturing, aiming to drive innovation and improve access to therapies with a focus on CAR-T cell immunotherapy [1–3]. An academic decentralized production network [4] of autologous CAR-T cells may offer numerous advantages compared to centralized production, including a shorter time from leukapheresis to patient infusion [5] lower costs, a more efficient supply chain, and the potential for fresh product administration [6], eliminating the need for cryopreservation, which is known to impact cell quantity and quality [7, 8]. To improve scalability and accessibility, the development of semi-automated systems by closed-system manufacturing technologies has become increasingly popular in academic settings [9, 10]. These advancements facilitate the broader implementation of CAR-T cell manufacturing,

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particularly for treating rare diseases that are not addressed by commercial CAR-T cell products [11–13]. However, despite the efficiencies provided by automated bioreactors and closed systems, maintaining strict quality control remains a significant challenge [14].

Effective management of raw materials, reagents, and consumables (RMRCs) is critical in CAR-T cell production, as it directly impacts the final product's quality, efficacy, and safety. [15, 16]. Variations in RMRCs' quality can compromise drug stability and potency, affecting yield, reproducibility, and production costs. Inadequate control of RMRCs not only raises the risk of defective batches and production failures but may also translate into adverse clinical outcomes, particularly treatment-related toxicities. Rigorous RMRCs management, including traceability and risk-based quality control, is therefore essential to prevent adverse effects or toxicity issues.

Management of raw materials is defined in Good Manufacturing Practices (GMP), ICH Q10 guidelines, and section 5.2.12 of the European Pharmacopoeia, making it the responsibility of the manufacturing unit [17, 18]. However, limited data is available on the practical implementation of these requirements.

This work aims to streamline raw materials management and harmonizing RMRC management across French academic ATMP centers, for releasing autologous CAR-T cell batches in various academic CGT facilities that follow GMP guidelines for ATMP manufacturing [19, 20]. The European T2evolve consortium has conducted an initial analysis focusing specifically on raw material selection [21, 22]. Building on this work, we aim to expand the scope to encompass all processes related to RMRCs, including purchasing, quality control, release, storage, and usage [23, 24]. This project aims to assess the difficulties faced and the practices adopted in academic CGT facilities. Unlike previous position papers, which focused on material selection and QC testing, this study covers the full RMRC management workflow (from sourcing to deviation handling). It proposes collective, operational Quality Assurance (QA) measures. Based on this analysis, practical recommendations were formulated for managing RMRCs in academic CAR-T cell production units.

METHODOLOGY

The workshop was conducted following the methodology for harmonization of practices recommended by the Francophone Society of Bone Marrow Transplantation and Cellular Therapy (SFGM-TC) and the European Society for Blood and Marrow Transplantation (EBMT) [25].

After an initial workshop that focused on identifying the conditions and minimum requirements for the release of autologous fresh CAR T-cell products under hospital exemption [19], followed by a second workshop aimed at developing recommendations to harmonize key quality control tests for CAR T-cell batch release [20], The WP3-Bioproduction group of the UNITC Consortium has initiated a third workshop dedicated to RMRCs management.

Part IV of the Annex defines raw materials following Directive 2001/83/EC concerning the Code on Advanced Therapy Medicinal Products (ATMPs) for human use [26]. According to this definition, raw materials include any substance used in the manufacture of the medicinal product, encompassing all components of the medicinal product, as well as any consumables and packaging items that come into contact with the finished product. Reagents and consumables refer to all other substances and materials used in the production and quality control processes, including environmental control.

We provide a structured nationwide survey followed by a collaborative analysis, as part of this initiative, we evaluated the challenges and practices in RMRCs' management across the 11 production units of UNITC's GT3, which collectively represent all ANSM-approved personalized ATMP production units in France. An electronic survey was distributed to 7 academic platforms and the 4 ATMP platforms of the Établissement Français du Sang in France. The complete survey questionnaire is provided in the Supplementary Materials. The study aimed to assess the organization of RMRCs' management within academic production units. The analysis covered key aspects of RMRC management, focusing on the production unit characteristics, types of RMRC used, risk assessment, identified non-conformities and their distribution, consequences of anomalies, and strategies for improvement. This initiative aimed to assess the experiences of academic facilities over the past three years, gather essential insights, and enhance our understanding of the field. Workshop leaders performed comprehensive literature reviews to establish a robust foundation for subsequent discussions. The guidance statements were developed through three iterative online meetings and one in-person workshop. Participants included QA managers, production heads, and medical directors from all 11 centers. The in-person process culminated in a two-day in-person meeting held in Lille, France, in February 2025, during which this document was drafted. Draft recommendations were shared via collaborative documents and finalized by consensus.

MANAGING RMRC: EXPERIENCE FROM FRENCH ACADEMIC ATMP PRODUCTION SITES

Eleven French CGT facilities retrospectively reviewed their production activities over the past three years, from 2022 to 2024. Collected data showed that annual ATMP production per platform ranged from 5 to more than 20 (Fig. 1a). Over the three years, approximately one-third of platforms produced between 5 and 10 ATMPs annually, while another third produced between 10 and 20 ATMPs each year. In contrast, three centers (27%) reported higher production rates, manufacturing more than 20 units per year, which resulted in a shorter turnaround time between productions (less than 1 month compared to 1 to 3 months, data not shown). Academic CGT facilities exhibited a broad range of production expertise, including gene therapies, cell therapies, and tissue-engineered and combined ATMPs (Fig. 1a). Among the 11 surveyed centers, 9 produced at least two different types of ATMPs. In contrast, two centers specialized exclusively in a single ATMP category.

Subsequently, an assessment was conducted to map the references and suppliers involved in procuring RMRCs for the manufacture of ATMPs. The results showed that 6 out of 11 centers used more than 100 RMRC references, collaborating with over 30 suppliers (Fig. 1b). The remaining five centers used between 50 and 100 references, which can be explained by the fact that their production was limited to one or two types of ATMPs. Among all RMRC references, [1] out of 5 is classified as high-risk due to its direct impact on cell manufacturing. Interestingly, although each center employed distinct risk analysis methods (risk-ranking and filtering, Failure Mode Effects Analysis, and other criticality scoring systems), they all relied on the same core parameters. More than 70% of the surveyed platforms reported that their RMRC risk analysis was based on the following criteria: grade (Market Authorization, European Conformity label, Research Use Only, no status), biological properties (human, animal, recombinant or biological origin), contact between RMRC and intermediate/final product, presence of a certificate of analysis and sterility (microbial, endotoxin, mycoplasma contamination) (Fig. 1c).

Next, we asked the participating centers to conduct a comprehensive review of deviations associated with RMRCs encountered during ATMP manufacturing processes, including their root causes and impacts. Among all deviations related to ATMP production, those linked with RMRCs represented a small proportion, accounting for only 6.8%. However, in one out of three

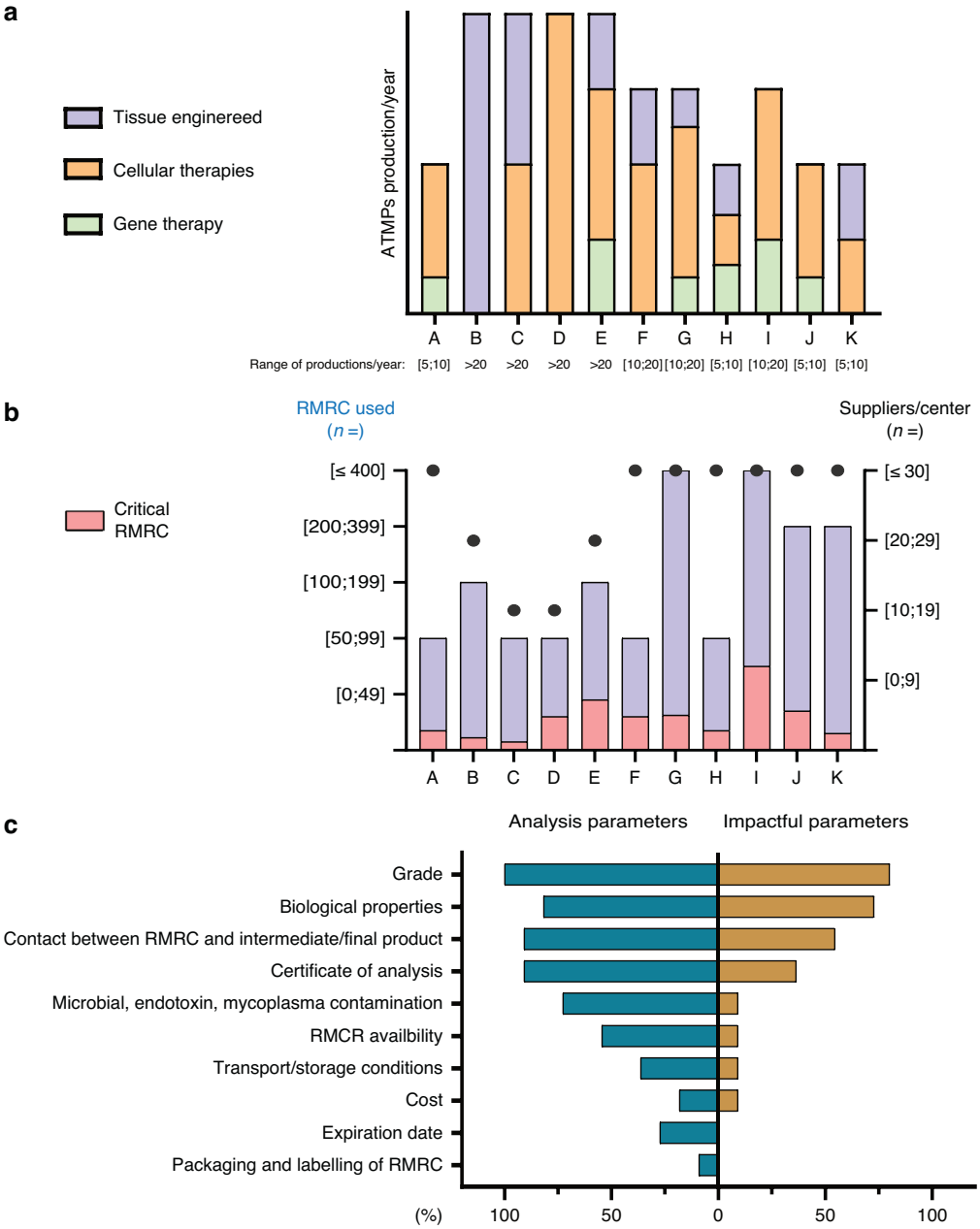

Fig. 1 Management of Advanced Therapy Medicinal Products (ATMP) in France from 2022 to 2024. a Repartition of ATMPs production per year for each production center (mean of the previous three years), where the number of productions 'n', for each ATMP category, is given according to a range. **b** RMRCs management summarized by the number of references, suppliers, and the proportion of critical RMRCs amongst all RMRCs for each center. **c** Bar graph representing the proportion of risk analysis parameters defined and most used by the different production centers for the RMRC's risk profiling. ATMPs: Advanced Therapies Medicinal Products, RMRCs: Raw Materials, Reagents, Consumables. ATMPs' production centers were anonymized by assigning each a unique letter.

cases, these RMRCs related deviations triggered the initiation of a change management process, involving additional human resources, increased costs, and the need to modify processes with regulatory authorities (mean 28,3%; range [5;70]) (Fig. 2a). The most frequent areas affected by RMRC-related deviations were stock shortages (70%), reference changes (64%), use issues (46%), anomalies related to receipt or quarantine/release (36%), and ordering-related anomalies (27%) (Fig. 2b). The most critical deviations mirrored the most frequent domains (Fig. 2b). The results obtained from the survey data did not reveal any consequences for the drug product or the patient, highlighting the robust quality assurance management in the bioproduction centers. Taken together, these findings highlight the primary causes of RMRC-related deviations and emphasize the recurrence of these issues across centers, underscoring the need for collective reflection and the implementation of shared preventive measures. Finally, each center assessed its effectiveness in implementing several key measures to reduce the recurrence of RMRC-related deviations, including supplier audits, the availability of backup references, functional testing, and sampling for the most critical RMRCs. Functional tests and sampling of critical RMRCs were more efficiently established with optimal implementation by 73% and 64% of centers, respectively (Fig. 2c). In contrast, the back-up measure for critical RMRCs was poorly implemented, with 64% of responding centers reporting inadequate application of this action.

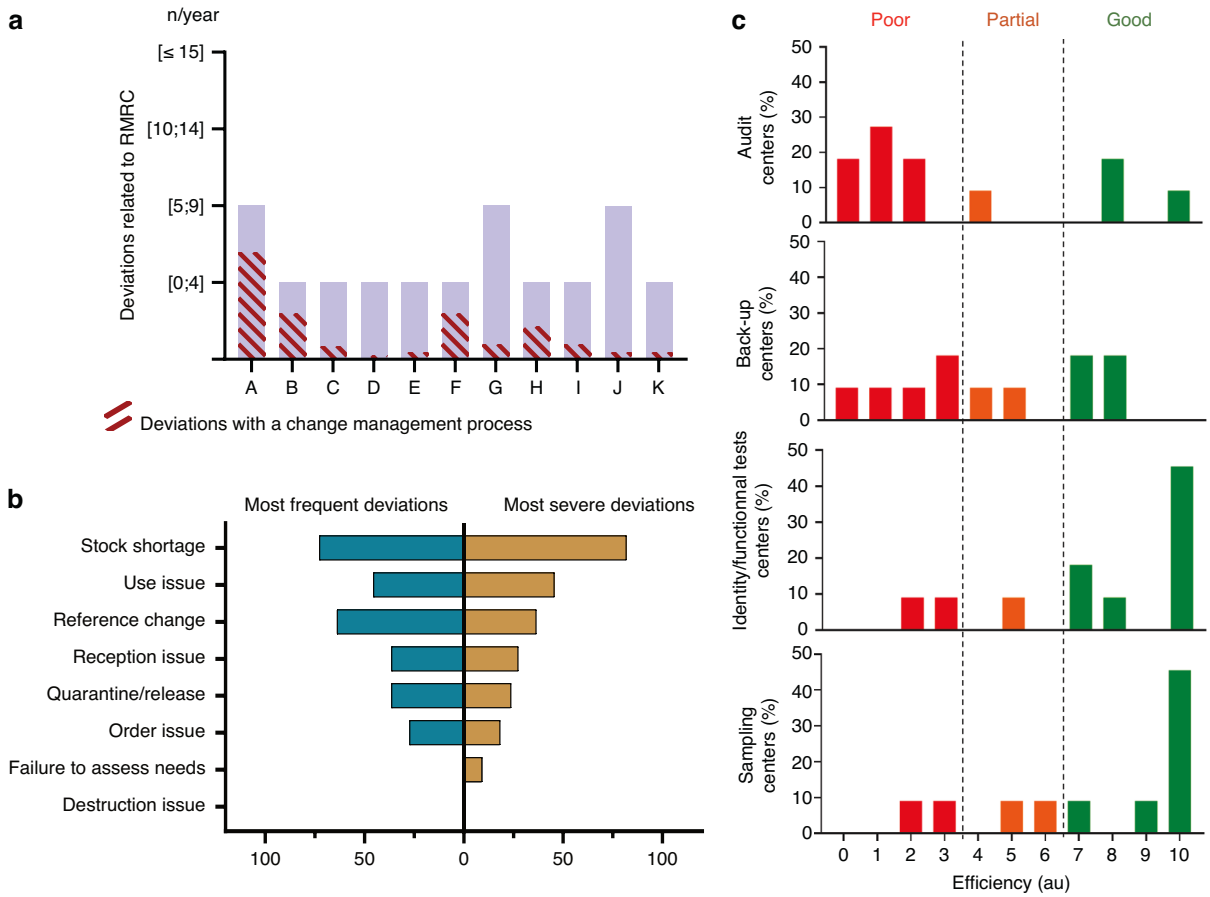

Fig. 2 RMRC-Related Constraints and Management Strategies With Proposed Solutions. a Proportion of RMRC-related deviations initiating changes amongst all the deviations related to RMRCs for each center. **b** Bar graph representing the proportion of the most frequent and most severe deviation domains about RMRC management. RMRCs: Raw Materials, Reagents, Consumables. The ATMP centers were anonymized by assigning each a unique letter. **c** Graphical representation of the different actions implemented by ATMPs production centers to limit the recurrence of RMRC-related deviation. The implementation capacity of these actions is evaluated on a scale of 1 to 10, measured in arbitrary units on the x-axis. The scores from 1–10 were self-assessed by centers (Scores 0–3 = poor implementation, 4–6 = partial, 7–10 = good).

GUIDELINES FOR ACADEMIC ATMP PRODUCTION FACILITIES

The Bioproduction Working Group of the UNITC Consortium approved its guidance in February 2025, comprising three final guidance statements and a flow diagram for risk analysis specific to CAR-T cell manufacturing.

Our study complements ongoing European initiatives aimed at harmonizing ATMP development and regulation. In particular, we now reference the DARE-NL WP2 program, which focuses on establishing a national infrastructure for ATMP development in the Netherlands, as well as the GoCART Coalition, which promotes collaboration and standardization across European CAR-T academic centers. These initiatives, alongside the previously cited T2EVOLVE consortium, share common goals with our national French network, notably in risk-based quality management, decentralized manufacturing models, and regulatory alignment. Our data-driven recommendations, based on real-world academic manufacturing practices, offer a practical framework that could be aligned with these European efforts to build a more resilient, coordinated ATMP ecosystem across borders.

Our workshop established parameters for standard risk analysis regarding RMRC management. This framework enables the determination of risk-based actions to address deviations and ensure product quality. As management of RMRCs becomes increasingly complex, adopting a harmonized and collaborative approach across centers is essential [27]. The following recommendations aim to enhance the efficiency, quality, and flexibility of the staff regarding the quality management system.

Harmonization between centers

Common RMRC classification framework. We propose a unified RMRC classification system based on a shared risk criterion [28], enabling consistent identification of critical RMRCs across centers (Fig. 3). By adopting a shared risk-based approach, centers can prioritize actions and calibrate control levels. Critical RMRCs are determined by the lack of available clinical grade (market authorization, European conformity label), the biological source (either human or animal), and their close association with intermediate products (like selection beads, tubing sets, activation beads) as well as final products (such as albumin, media, and bags of the final drug product). Moreover, the absence of a certificate of analysis or confirmation of sterility (including checks for microbial culture, endotoxin, and mycoplasma contamination) is an additional indicator of critical RMRCs. The vector, as a starting material, is examined separately from this analysis.

Harmonize RMRC management measures. Key management practices should be standardized to ensure consistent handling of high-risk RMRCs, including functional or identity testing protocols, sampling strategies, and the definition and qualification of back-up references. This harmonization will minimize performance disparities and improve overall process security. Functional testing and back-up references should be prioritized for critical RMRC that affect cell functionality (activation beads, medium, cytokines, transduction enhancers, etc.) during the bioproduction process, especially for reference changes or stock shortages.

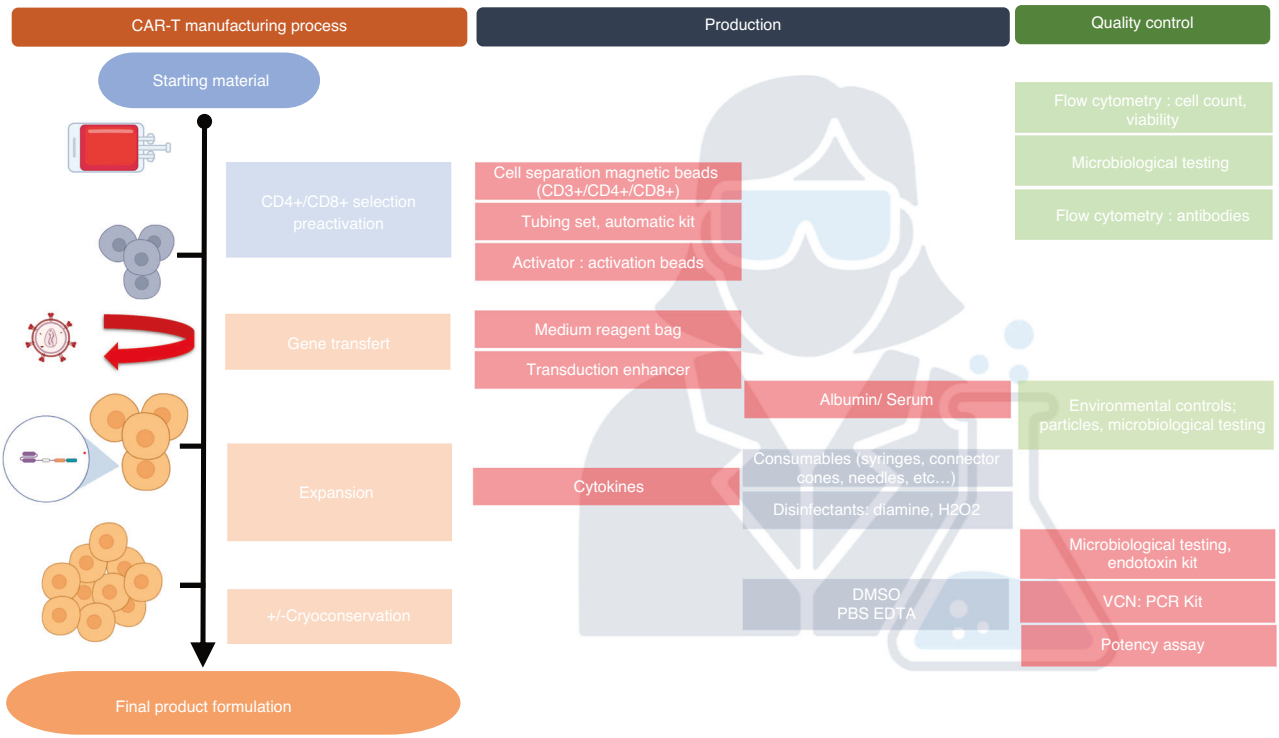

Fig. 3 RMRC classification framework: Overview of the CAR-T cell manufacturing process, including production steps and quality control measures. Elements highlighted in red correspond to RMRCs identified as having a high-risk level (in red) according to risk analysis. Deviations involving high-risk RMRCs, such as sterility issues or supplier changes, has to trigger contingency measures, including emergency change controls, validated alternatives, and real-time release strategies. These actions have to be conducted in accordance with each center's internal QA procedures.

Sampling strategy must ensure representativeness of the batch for raw materials, packaging items, or products from which they are taken. RMRC samples primarily concern packaging items; they must be kept for the same duration as the finished product in question. Nevertheless, as specified in GMP guidelines (part IV, chapter 12, paragraph 12.2), small production processes do not have any mandatory requirements for reference sampling (i.e., autologous sample for one patient, one treatment strategy).

Strengthen inter-academic center collaboration

Mutualise key quality assurance activities. Several Quality Assurance (QA) actions can be shared to enhance efficiency and reduce redundancy. We have identified three priorities: joint supplier audits, shared alert systems and corrective actions, and unified change control validation processes. Pooling these efforts will strengthen collective quality oversight while optimizing resource utilization.

Optimize non-conformity management. Developing shared tools and processes will foster stronger collaboration among centers. This is especially valuable for centers with limited resources or lower production capacity, as it enables them to benefit from the collective expertise and infrastructure of the network.

Harmonizing deviation reporting and analysis systems will reduce administrative burdens and enhance responsiveness. A unified approach will allow for faster issue resolution and enable more strategic use of data for preventive actions.

Encourage the creation of a national RMRC database

The establishment of a national database or centralized resource hub for critical RMRCs, qualified suppliers, and validated management practices is strongly recommended. This initiative would support informed decision-making, promote continuous improvement, and enhance center coordination [29]. Such an initiative will significantly strengthen our partnerships with regulatory agencies [30], fostering greater transparency regarding the challenges we face. It will also clearly demonstrate our unwavering commitment to making meaningful improvements in the community and our dedication to achieving substantial progress.

By pursuing these recommendations, French ATMP centers can streamline their internal processes and reinforce the overall robustness and agility of the national bioproduction ecosystem, ensuring sustained compliance and patient safety while optimizing the use of available resources.

CONCLUSION

This national multicenter study, encompassing all French academic ATMP production platforms over three years, provides valuable insight into current practices for managing RMRCs. Despite variability in production volumes and ATMP types, all centers demonstrated a shared understanding of RMRC criticality and converged on similar risk analysis criteria, highlighting the maturity and consistency of QA processes across the network.

Notably, while RMRC-related deviations accounted for only 6.8% of total deviations, they frequently triggered significant consequences, such as initiating change management procedures, requiring additional human resources, and necessitating additional regulatory authorizations. These observations emphasize the need for more efficient and proactive RMRC management. The absence of impacts on drug product quality or patient safety attests to the robustness of existing QA systems within participating centers.

However, several areas for improvement have been identified. The implementation of specific RMRC management measures, particularly the use of back-up references and supplier audits, remains suboptimal and inconsistently applied across centers. Functional testing and sampling of critical RMRCs were more

widely and effectively adopted, but even these practices could benefit from further harmonization.

The homogeneous distribution of responses across academic platforms suggests that the challenges are widely shared and therefore call for a collective and coordinated approach. As such, this study highlights the need for national-level harmonization and mutualization of risk-based strategies and RMRC management procedures.

DATA AVAILABILITY

The datasets generated during and/or analysed during the current study are available in the Figshare repository, https://doi.org/10.6084/m9.figshare.29679044.

REFERENCES

1. Trias E, Juan M, Urbano-Ispizua A, Calvo G. The hospital exemption pathway for the approval of advanced therapy medicinal products: an underused opportunity? The case of the CAR-T ARI-0001. Vol. 57, Bone Marrow Transplant. Springer Nature; 2022. p. 156–9.
2. Egri N, Ortiz de Landazuri I, San Bartolomé C, Ortega JR, Español-Rego M, Juan M. CART manufacturing process and reasons for academy-pharma collaboration. Vol. 217, Immunology Letters. Elsevier B.V.; 2020. p. 39–48.
3. Dias J, Garcia J, Agliardi G, Roddie C. CAR-T cell manufacturing landscape—Lessons from the past decade and considerations for early clinical development. Vol. 32, Molecular Therapy Methods and Clinical Development. Cell Press; 2024.
4. Shah M, Krull A, Odonnell L, de Lima MJ, Bezerra E. Promises and challenges of a decentralized CAR T-cell manufacturing model. Frontiers in Transplantation. 2023 Sep;2.
5. Liu Y, Sperling AS, Smith EL, Mooney DJ. Optimizing the manufacturing and antitumour response of CAR T therapy. Nat Rev Bioeng. 2023;1:271–85.
6. Odstrcil MS, Lee CJ, Sobieski C, Weisdorf D, Couriel D. Access to CAR T-cell therapy: Focus on diversity, equity and inclusion. Vol. 63, Blood Reviews. Churchill Livingstone; 2024.
7. Juan M, Delgado J, Calvo G, Trias E, Urbano-Ispizua Á. Is hospital exemption an alternative or a bridge to european medicines agency for developing academic chimeric antigen receptor T-Cell in Europe? Our experience with ARI-0001. Hum Gene Ther. 2021;32:1004–7.
8. Le Guen C, Grain A, Le Calvez B, Saiagh S, Vrignaud F, Eveillard M, et al. Can academic structures improve access to CAR-T cells? Vol. 111, Bulletin du Cancer. John Libbey; 2024. p. 62–72.
9. Fury B, Bauer G. GMP manufacturing of cell and gene therapy products: Challenges, opportunities, and pathways forward. Molecular Therapy. Cell Press; 2025.
10. Adair JE, Waters T, Haworth KG, Kubek SP, Trobridge GD, Hocum JD, et al. Semi-Automated closed system manufacturing of lentivirus gene-modified haematopoietic stem cells for gene therapy. Nat Commun. 2016 Oct;7.
11. Gee AP. Manufacturing genetically modified T cells for clinical trials. Vol. 22, Cancer Gene Therapy. Nature Publishing Group; 2015. p. 67–71.
12. Aleksandrova K, Leise J, Priesner C, Aktas M, Apel M, Assenmacher M, et al. Automated manufacturing and characterization of clinical grade autologous CD20 CAR T cells for the treatment of patients with stage III/IV melanoma. Front Immunol. 2024;15:1328368.
13. Trainor N, Purpura KA, Middleton K, Fargo K, Hails L, Vicentini-Hogan M, et al. Automated production of gene-modified chimeric antigen receptor T cells using the Cocoon Platform. Cytotherapy. 2023;25:1349–60.
14. Palani HK, Arunachalam AK, Kulkarni U, Yasar M, Venkatraman A, Palanikumar S, et al. Safety, efficacy and total cost of point-of-care manufactured anti-CD19 CAR-T cell therapy in India: VELCART trial. Mol Therapy Oncol. 2025 Jun;33.
15. Aijaz A, Li M, Smith D, Khong D, Leblon C, Fenton OS, et al. Biomanufacturing for clinically advanced cell therapies. Vol. 2, Nat Biomed Eng. Nature Publishing Group; 2018. p. 362–76.
16. Watanabe N, Mo F, McKenna MK. Impact of Manufacturing Procedures on CAR T Cell Functionality. Vol. 13, Front Immunol. Frontiers Media S.A.; 2022.
17. EMA- multidisciplinary-guidelines.
18. ANSM- GUIDE DES BONNES PRATIQUES DE FABRICATION.
19. Boyer O, Bensoussan D, Bönig H, Chabannon C, Clémenceau B, Cuffel A, et al. Identification of the conditions and minimum requirements necessary for the release of autologous fresh CAR T-cell products under hospital exemption: a position paper from the WP-bioproduction of the UNITC consortium. Bone Marrow Transplant. 2025 Apr;
20. Marton C, Clémenceau B, Dachy G, Demerle C, Derenne S, Ferrand C, et al. Harmonisation of quality control tests for academic production of CAR-T cells: a position paper from the WP-bioproduction of the UNITC consortium. Bone Marrow Transplant. 2025 May; Available from: https://www.nature.com/articles/s41409-025-02637-8.
21. Navarro S, Moukheiber C, Inogés Sancho S, Ruiz Guillén M, López-Díaz de Cerio A, Sanges C, et al. Optimizing CAR-T treatment: A T2EVOLVE guide to raw and starting material selection. Molecular Therapy. Cell Press; 2024.
22. De Angelis B, D'Amore ML, Lecot P, Neininger K, Lorrain M, Gambotti L, et al. European survey on CAR T-Cell analytical methods from apheresis to post-infusion immunomonitoring. Front Immunol. 2025;16.
23. ten Ham RMT, Hoekman J, Hövels AM, Broekmans AW, Leufkens HGM, Klungel OH. Challenges in advanced therapy medicinal product development: a survey among companies in Europe. Mol Ther Methods Clin Dev. 2018;11:121–30.
24. Sanchez-Guijo F, Vives J, Ruggeri A, Chabannon C, Corbacioglu S, Dolstra H, et al. Current challenges in cell and gene therapy: a joint view from the European Committee of the International Society for Cell & Gene Therapy (ISCT) and the European Society for Blood and Marrow Transplantation (EBMT). Cytotherapy. 2024;26:681–5.
25. Yakoub-Agha I, Greco R, Onida F, de la Cámara R, Ciceri F, Corbacioglu S, et al. Practice harmonization workshops of EBMT: an expert-based approach to generate practical and contemporary guidelines within the arena of hematopoietic cell transplantation and cellular therapy. Bone Marrow Transplant. 2023;58:696–700.
26. Directive 2001/83/EC, Part IV.
27. Nikiforow S, Frigault MJ, Frey NV, Gardner RA, Komanduri KV, Perales MA, et al. Paving the road for chimeric antigen receptor T cells: American Society for Transplantation and Cellular Therapy 80/20 task force consensus on challenges and solutions to improving efficiency of clinical center certification and maintenance of operations for commercially approved immune effector cell therapies. Transpl Cell Ther. 2023;29:228–39.
28. Shi J, Yang J, Zheng Y, Hong Wong PH, Hu H, Lam Ung CO. The clinical quality management system of advanced therapy medicinal products in the hospital setting: a scoping review. Mol Ther Methods Clin Dev [Internet]. 2025 May;101485. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2329050125000804.
29. Wu X, Cadinanos-Garai A, Quach V, Jurado E, Vaissié A, Abou-el-Enein M. Redefining quality in cell and gene therapies: Lessons from implementing electronic QMS in academic cGMP facility. Molecular Therapy. Cell Press; 2025.
30. Tanaka T, Karasawa H, Yasumoto M, Choi BH, Chang R, Komuro M, et al. Non-clinical, quality and environmental impact assessments of cell and gene therapy products: Report on the 5th Asia Partnership Conference of Regenerative Medicine - April, 2022. 25, Cytotherapy. Elsevier B.V.; 2023. p. 683–98.

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AUTHOR CONTRIBUTIONS

UC, JG, JSD, and IYA conceptualized the subject for this workshop; IYA developed the methodology; all authors participated in the teleconferences (UC, JG, CA, CM, BC, SD, ST, FS, JV, AM, HR, KT, GD, CD, BCA, CC, LR, EF, SV, DB, JDV, AG, CDO, HB, EM, MC, JRF, JL, MD, CF, CG, JSD, JM, OB, and IYA). UC, JG, CA, CM, BC, LR, IYA, CG, and JSD participated in the face-to-face meeting and wrote the original manuscript draft. CM, UC, JSD, HB, BCA, CG, CE, IYA. DB, CC, MD, JDV, JSD, AD, EF, JG, ST, AG, JL, LR, and SV reviewed and edited the manuscript. JSD edited the final manuscript, and all authors approved it. After the survey responses had been analyzed, the extracted data were presented and discussed during three dedicated meetings involving all contributing authors. These meetings served to review the survey findings, prioritize key topics, and formulate draft guidance statements. The recommendations were iteratively developed throughout these discussions and then drafted in written form by JSD and UC. The draft manuscript, including the proposed recommendations, was circulated among all authors for comments and corrections using tracked changes, ensuring that every contributor had the opportunity to provide input. Subsequent revisions were made based on this collective feedback. A final version of the manuscript, incorporating all agreed-upon modifications, was then reviewed during a video conference with all authors present. During this meeting, the guidance statements were discussed point by point, endorsed by consensus, and formally approved by the entire group of authors.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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