

Future Trends in Drug and Medical Device Integration

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ABSTRACT

Drug and medical device integration has advanced from mechanically combined products (tablet + plastic blister packaging, vial + syringe) to genuinely integrated biomedical systems where the pharmacological and device components are inseparable contributors to therapeutic effect. The trajectory across the past two decades includes drug-eluting stents that transformed cardiovascular intervention, closed-loop insulin delivery systems that are redefining diabetes care, device-delivered advanced therapy medicinal products that enable cell and gene therapy at clinical scale, digital therapeutics that deliver therapeutic intervention through software, and emerging categories including electroceutical combinations, theranostic drug-device pairs, and AI-personalised combination therapies where the therapeutic regimen adapts to individual patient physiology. Looking forward, several trend vectors are converging to reshape combination product development: AI-enhanced personalisation of both drug and device components, manufacturing technology convergence including 3D printing and continuous manufacturing, regulatory framework maturation for novel combination product categories, and increased emphasis on real-world evidence generation throughout the combination product lifecycle. This review synthesises current and emerging drug-device integration trends across five dimensions: technological convergence trends reshaping combination product architecture, regulatory framework evolution accommodating novel combination product categories, clinical evidence generation advances supporting combination product development, manufacturing technology trends enabling new combination product categories, and commercial and access trends affecting combination product availability and affordability. For each dimension, the review synthesises current status, near-term trajectory (2025-2028), medium-term horizon (2028-2032), and key uncertainty factors that will determine actual outcome paths. The review synthesises findings across the 33 comparative framework studies published in this journal during 2024-2025 that form the empirical evidence base for the trend analysis.

Keywords: drug-device integration; combination products; future trends; AI-enhanced personalisation; 3D printing pharmaceutical; regulatory evolution; real-world evidence; digital therapeutics; electroceutical combinations; theranostics; advanced therapy medicinal products; continuous manufacturing

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1. Introduction

1.1 The Drug-Device Integration Trajectory

Medicine has been combining drugs and devices since antiquity -- the earliest medical practitioners delivered medicinal preparations through rudimentary applicators and devices -- but the modern era of deliberate drug-device integration can be traced to the introduction of coronary drug-eluting stents in the early 2000s. The DES paradigm demonstrated that combining a pharmacological agent (antiproliferative drug) with a device (metallic stent) could produce clinical outcomes that neither component achieved alone: the stent provided mechanical patency, the drug prevented neointimal hyperplasia, and the combination transformed coronary intervention outcomes in ways that bare metal stents alone could not. The subsequent two decades have produced a progressively richer landscape of combination products. Insulin pumps integrated with continuous glucose monitors evolved into closed-loop systems that now approach the functionality of an artificial pancreas. Drug-eluting embolic beads for hepatocellular carcinoma combined targeted drug delivery with vascular occlusion. Photodynamic therapy systems coordinated photosensitiser drug administration with targeted light delivery. Cell and gene therapy delivery systems enabled autologous and allogeneic cell therapies at clinical scale through specialised infusion and monitoring infrastructure. Digital therapeutics extended the combination product concept to software-delivered therapy authorised through prescription digital therapeutic regulatory pathways. Looking forward, several convergent trend vectors are reshaping what drug-device integration means. AI-enhanced personalisation is extending from device-side optimisation to combined drug-device regimen adaptation. 3D printing and continuous manufacturing technologies are enabling patient-specific and on-demand combination product manufacturing. Regulatory frameworks continue to evolve to accommodate novel combination product categories. Real-world evidence is becoming an increasingly central component of combination product evaluation throughout the product lifecycle. This review synthesises these trends into a structured forecast of combination product development trajectory over the 2025-2032 horizon.

1.2 Review Scope and Methodology

This review synthesises findings across the 33 comparative framework studies published in this

journal during 2024-2025, each addressing a specific combination product methodology domain -- from biocompatibility testing models and controlled release polymers to regulatory surveillance frameworks and stability study design approaches. The cumulative evidence base from these studies provides the empirical foundation for trend analysis that would be difficult to construct from any single methodology assessment. Five trend dimensions structure the analysis: technological convergence reshaping combination product architecture, regulatory framework evolution accommodating novel categories, clinical evidence generation advances, manufacturing technology trends enabling new product categories, and commercial and access trends affecting availability. For each dimension, the review describes current status, identifies near-term trajectory (2025-2028), forecasts medium-term horizon (2028-2032), and surfaces the key uncertainty factors that will determine actual outcome paths. The review concludes with cross-dimensional synthesis and implications for combination product development strategy, regulatory framework evolution, and clinical deployment planning.

2. Technological Convergence Trends

2.1 AI-Enhanced Combination Product Personalisation

The personalisation trend vector has progressed from device-side personalisation (pacemaker programming, insulin pump basal rate profiles) to integrated combination product personalisation where both drug and device parameters adapt to individual patient physiology. Closed-loop insulin delivery represents the most mature integrated personalisation example, with algorithms that adjust insulin delivery continuously based on CGM feedback and that learn individual patient response patterns over time. AI-personalised oncology infusion therapy extends this model to chemotherapy, where ML algorithms integrate patient-specific pharmacokinetic data, tumour response indicators, and toxicity monitoring to generate individualised regimen recommendations. Over the 2025-2028 near-term, AI-enhanced personalisation is likely to extend to additional combination product categories where suitable physiological biomarkers support real-time adjustment: intrathecal drug delivery responding to biomarkers of spasticity or pain, deep brain stimulation combined with pharmacological therapy in Parkinson's disease with AI-coordinated regimen adjustment, and

extended-release drug delivery systems with responsive release modulation based on continuous biomarker feedback. Over the 2028-2032 medium-term, fully integrated combination products with AI coordination of drug selection, dose, and delivery parameters based on multi-modal patient data are plausible for specific therapeutic areas where evidence infrastructure supports the required algorithm training and validation.

2.2 Digital Therapeutic Integration and Electroceutical Combinations

Digital therapeutics have established themselves as a distinct combination product category over the past five years, with prescription digital therapeutics authorised by FDA De Novo and EU MDR pathways covering mental health, chronic disease self-management, and substance use disorders. The near-term trajectory extends digital therapeutic deployment to additional indication categories and increases integration with pharmaceutical therapy, creating drug-digital therapeutic combinations where the software intervention and the drug produce complementary therapeutic effects. Electroceutical combinations represent a newer frontier where electrical field therapy, bioelectronic medicine approaches, and pharmacological agents are combined to produce clinical effects that neither component achieves alone. Tumour-treating fields therapy for glioblastoma combined with temozolomide chemotherapy provides the commercial precedent; the broader pipeline includes vagus nerve stimulation combined with pharmacotherapy for inflammatory conditions, spinal cord stimulation combined with opioids for chronic pain, and emerging electroceutical-pharmacological combinations for metabolic disease. Over the 2028-2032 horizon, electroceutical-pharmaceutical combinations are likely to expand substantially as the bioelectronic medicine field matures and clinical evidence generation for combination effects accumulates. The principal uncertainty is whether regulatory pathways for electroceutical-drug combinations will mature at the pace required to support expected clinical development programmes.

Table 1: Technological Convergence Trends in Drug-Device Integration

Trend Dimension	2025 Current Status	2025-2028 Near-term	2028-2032 Medium-term
AI-personalised combination	CGM-insulin closed-loop standard	AI oncology infusion expansion	Multi-modal AI combination regimens
Digital therapeutic integration	PDT standalone + drug-DTx pilots	Drug-DTx combination products	Integrated digital-pharmaceutical categories
Electroceutical combinations	TTF fields + temozolomide only approved	VNS + drug pipeline development	Broader electroceutical-drug approvals
Theranostic combinations	PSMA radio nuclides established	Extended targeting chemistries	Multi-target theranostic platforms
Advanced manufacturing	GMP 3D printing emerging	Hospital pharmacy 3D printing pilots	Distributed personalised manufacturing
Continuous manufacturing	Pharmaceutical CM established	Combination product CM pilots	Integrated drug-device CM standard

PDT = Prescription Digital Therapeutic; DTx = Digital Therapeutic; TTF fields = Tumour Treating Fields; VNS = Vagus Nerve Stimulation; PSMA = Prostate-Specific Membrane Antigen; GMP = Good Manufacturing Practice; CM = Continuous Manufacturing.

3. Regulatory Framework Evolution

3.1 Primary Regulatory Pathway Maturation

The regulatory landscape for combination products has evolved substantially over the past decade and continues to develop. The 2024-2025 comparative framework studies published in this journal documented that structured BRAT-EMA benefit-risk frameworks achieved the highest regulatory acceptance for combination product submissions, while EU MDR Article 117 integrated assessment and FDA OCP integrated combination product safety assessment represent the structural frameworks that are progressively accommodating combination product evaluation across both US and EU markets. The near-term 2025-2028 trajectory includes continued maturation of EU MDR Article 117 implementation as notified body expertise deepens through accumulated case experience, expansion of FDA OCP integrated assessment capability to novel combination product categories including electroceutical combinations and AI-personalised regimens, and initial regulatory pathway development for drug-digital therapeutic combinations where the software component and the drug component are

clinically integrated. The Germany DiGA Fast-Track model for prescription digital therapeutics is likely to inspire similar reimbursement-linked authorisation frameworks in Austria, France, and Belgium, with possible extension to drug-digital therapeutic combination products as precedent accumulates.

3.2 International Harmonisation and AI Integration

International regulatory harmonisation through IMDRF continues to progress, with the Adverse Event Terminologies providing the coding infrastructure for cross-jurisdictional surveillance, the Patient Registries working group advancing global registry coordination, and the Software as a Medical Device framework addressing regulatory convergence for software-based combination products. The near-term 2025-2028 trajectory includes continued IMDRF guidance development for specific combination product categories, with probable extension to cover AI-enhanced combination products and advanced therapy medicinal product categories. AI integration in regulatory decision-making represents one of the most consequential regulatory evolution vectors. The current regulatory pathway for AI-enhanced combination product evidence -- AI-based pooled safety analysis, AI-enhanced stability prediction, AI clinical outcome prediction models -- requires case-by-case scientific advice engagement because formal guidance is incomplete. The 2028-2032 medium-term horizon is likely to include substantial regulatory guidance development for AI in combination product submissions, with probable FDA Innovative Science and Technology Approaches programme extensions and EMA scientific guidance development that together would reduce the regulatory uncertainty currently limiting AI-enhanced evidence deployment as primary combination product evaluation evidence. The principal uncertainty is the pace of regulatory guidance development, which depends on accumulated validation evidence and regulatory authority resource allocation to AI regulatory science.

Table 2: Regulatory Framework Evolution Trends

Framework Dimension	2025 Current Status	2025-2028 Near-term	Key Uncertainty
EU MDR Article 117	Article 117 implementation ongoing	Implementation maturation; NB expertise	Notified body capacity

Framework Dimension	2025 Current Status	2025-2028 Near-term	Key Uncertainty
FDA OCP integrated review	Mature for established categories	Extension to novel combination categories	Novel category review timelines
Digital therapeutic pathways	DiGA, De Novo, NICE ESF operational	EU/national DiGA-style expansion	Drug-DTx combination precedent
AI in regulatory evidence	Case-by-case scientific advice	Formal guidance development (FDA/EMA)	Pace of guidance development
IMDRF harmonisation	AETs, patient registries, SaMD WG	Combination product-specific IMDRF work	Jurisdictional adoption pace
RWE in regulatory evaluation	ATMP + specific categories	Systematic RWE expectations	Data infrastructure maturation

NB = Notified Body; OCP = Office of Combination Products; DiGA = Digitale Gesundheitsanwendungen (Germany's digital health applications fast-track pathway); ESF = Evidence Standards Framework; AETs = Adverse Event Terminologies; WG = Working Group; RWE = Real-World Evidence; ATMP = Advanced Therapy Medicinal Product.

4. Clinical Evidence Generation Trends

4.1 Real-World Evidence Integration and Transparency

Real-world evidence integration in combination product evaluation has progressed from supplementary supporting evidence to, in specific contexts, primary evidence supporting regulatory submissions. The ATMP context provides the clearest example: cell and gene therapy programmes with small pre-market clinical trial populations routinely include structured post-market evidence generation plans where real-world outcomes complement pre-market evidence in establishing the product's benefit-risk profile. The near-term trajectory extends RWE integration to additional combination product categories where pre-market evidence limitations make post-market data particularly valuable. Clinical trial transparency continues to strengthen through EU MDR Article 92 requirements for implantable and Class III device clinical investigation summaries, ICMJE data sharing requirements, and evolving AI-enhanced real-time data access portals with privacy-preserving analytics. The medium-term 2028-2032 horizon is likely to include substantial expansion of continuous trial data access models that enable

independent researchers, regulatory authorities, and clinician users to query trial data throughout the trial lifecycle rather than only after completion and publication. The standardisation of IPD sharing governance for combination product trials -- building on pharmaceutical sector precedent -- is a probable regulatory infrastructure development that would increase secondary research output from combination product clinical programmes.

4.2 Digital Biomarkers and AI-Generated Endpoints

Digital biomarker integration in combination product clinical evaluation represents one of the most consequential evidence generation trends. Device-derived telemetry (CGM data, implantable pump delivery records, pacing impedance trends) provides continuous clinical performance data that periodic assessment cannot match, and AI models integrating multi-source digital biomarker data generate composite performance metrics that individual measurements cannot capture. The near-term trajectory extends digital biomarker validation for regulatory use as co-primary endpoints in specific combination product categories, with FDA Biomarker Qualification Programme extensions likely to provide the regulatory framework for broader adoption. AI-generated performance prediction models that integrate multiple endpoint streams -- clinical outcomes, device telemetry, patient-reported data, imaging -- to generate composite performance estimates represent an emerging evidence category whose regulatory acceptance is currently limited but growing. The 2028-2032 medium-term horizon is likely to include regulatory qualification methodology for AI-generated composite endpoints, with specific combination product categories where the multi-modal integration provides substantial clinical value being early adopters. The principal uncertainty is the regulatory acceptance pace, which depends on accumulated validation evidence and regulatory framework development.

5. Manufacturing Technology and Commercial Trends

5.1 3D Printing, Continuous Manufacturing, and Advanced Therapy Production

Manufacturing technology trends are reshaping combination product production in ways that expand the feasible product design space. 3D printing of pharmaceutical and combination products has progressed from Spritam's 2015 first-approved 3D-printed drug product to a small

but expanding portfolio of 3D-printed pharmaceutical applications, with paediatric dose individualisation representing the most active clinical application area. The near-term 2025-2028 trajectory includes hospital pharmacy 3D printing pilots for paediatric and rare disease dose individualisation, with regulatory frameworks progressively accommodating point-of-care manufacturing. Continuous manufacturing extended from its pharmaceutical origins to combination products represents another transformative trend. Where conventional combination product manufacturing uses batch production with intermediate testing and quality release, continuous manufacturing enables real-time process analytical technology monitoring with quality attribute prediction from process parameters. For drug-eluting combination products where batch-to-batch variability is a clinical performance concern, continuous manufacturing offers substantial quality assurance improvements. Advanced therapy medicinal product manufacturing also continues to evolve, with allogeneic cell therapy platforms and distributed manufacturing models addressing the scalability constraints that autologous cell therapy faces.

5.2 Access, Affordability, and Sustainability

Commercial and access trends represent the most uncertain trend category but potentially the most consequential for actual patient benefit from combination product innovation. High-cost advanced therapy medicinal products -- CAR-T cell therapies at EUR 300,000-500,000 per patient, gene therapies at similar or higher prices -- raise access and affordability questions that healthcare systems globally are struggling to address. Outcome-based reimbursement models, risk-sharing agreements, and installment payment structures represent the principal commercial innovation responses, with varying adoption across healthcare systems. Sustainability considerations are becoming increasingly relevant for combination product development decisions. Environmental impact of single-use medical devices, carbon footprint of complex manufacturing supply chains, and end-of-life disposal considerations for combination products containing both drug and device components create sustainability challenges that pharmaceutical or device sustainability frameworks alone do not address. The 2028-2032 medium-term horizon is likely to include substantive regulatory expectations for combination product sustainability assessment,

with EU Medical Devices Regulation Annex I general safety and performance requirements providing an existing regulatory hook that could be expanded to incorporate environmental sustainability considerations.

Table 3: Manufacturing and Commercial Trends

Trend	2025 Status	2025-2028 Trajectory	2028-2032 Horizon
3D printing pharma/combo	Limited approved products	Hospital pharmacy pilots	Distributed personalised manufacturing
Continuous manufacturing	Pharma CM established	Combination product CM pilots	CM standard for high-volume combos
Allogeneic cell therapy	Early commercial products	Broader allogeneic CAR-T	Off-the-shelf alternatives to autologous
Outcome-based reimbursement	ATMP-focused agreements	Broader combination product	Standard for high-cost combos
Sustainability assessment	Voluntary and emerging	Regulatory integration beginning	Substantive regulatory expectations
Access harmonisation	National variation substantial	DiGA-style cross-border pilots	EU access framework convergence

CM = Continuous Manufacturing; CAR-T = Chimeric Antigen Receptor T-cell; ATMP = Advanced Therapy Medicinal Product; DiGA = Germany Digital Health Applications pathway.

Table 4: Cross-Dimensional Trend Priority Matrix

Dimension	Near-Term Priority (2025-2028)	Medium-Term Priority (2028-2032)
Technological	AI-personalised combination implementation	Electroceutical-pharmaceutical expansion
Regulatory	EU MDR Article 117 and AI evidence guidance	AI-enhanced combination products regulatory frameworks
Clinical evidence	RWE integration + digital biomarkers	AI-generated composite endpoints

Dimension	Near-Term Priority (2025-2028)	Medium-Term Priority (2028-2032)
Manufacturing	Hospital pharmacy 3D printing + CM pilots	Distributed personalised manufacturing
Commercial	Outcome-based reimbursement expansion	EU access framework harmonisation

Priority assessment based on synthesis of 33 comparative framework studies published in the journal during 2024-2025 covering combination product methodology domains.

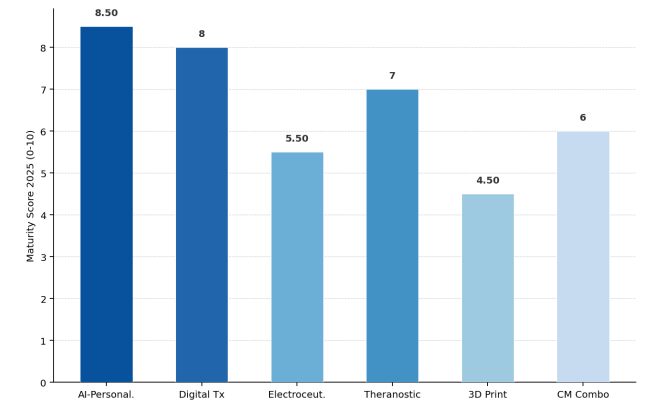


Figure 1: Technology Maturity Trajectory (Current to 2032 Projected)

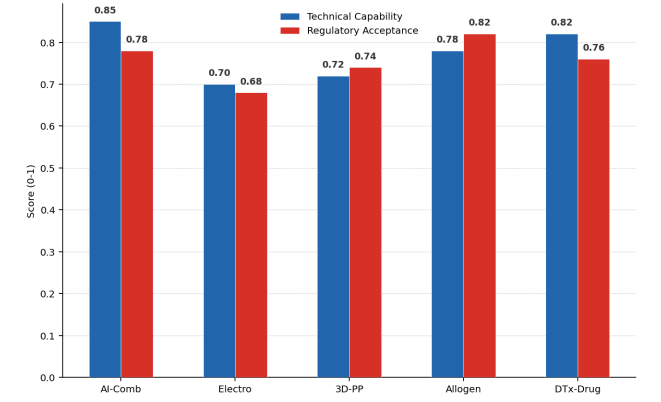


Figure 2: Regulatory Acceptance vs Technical Capability for Emerging Approaches

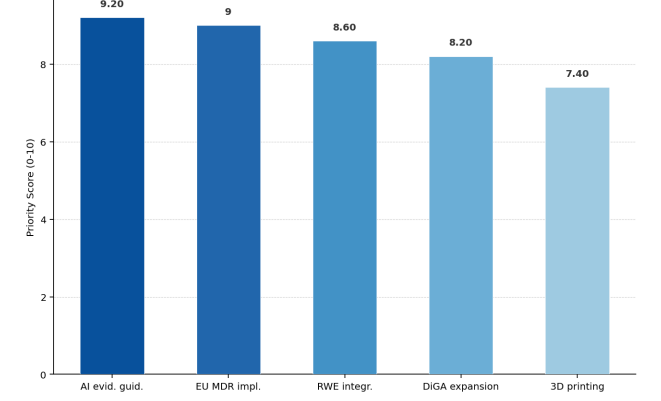


Figure 3: Near-Term Priority Ranking (2025-2028 Focus)

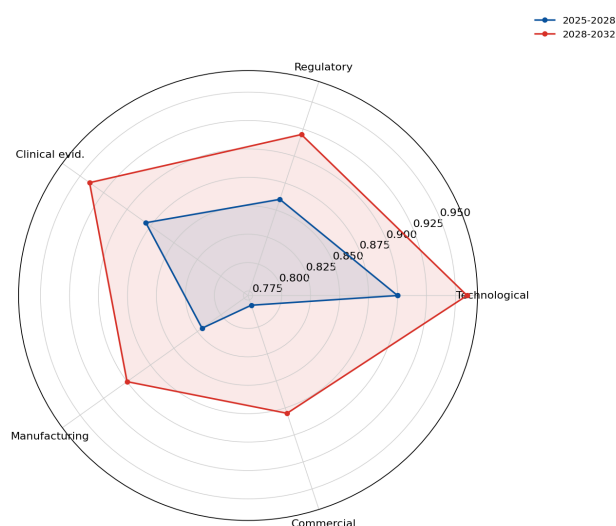


Figure 4: Five-Dimensional Trend Intensity Profile (2025-2032)

6. Conclusion

6.1 Synthesis and Strategic Implications

The trend synthesis across technological, regulatory, clinical evidence, manufacturing, and commercial dimensions suggests that combination product development is entering a phase of accelerating integration where the drug and device components become progressively more interdependent contributors to therapeutic effect. The near-term 2025-2028 priorities centre on implementation maturation of existing regulatory frameworks (EU MDR Article 117, FDA OCP integrated assessment), expansion of AI-enhanced personalisation to additional combination product categories, and regulatory pathway development for AI-enhanced evidence in regulatory submissions. The medium-term 2028-2032 horizon is likely to include broader regulatory acceptance of AI-generated composite endpoints, substantial electroceutical-pharmaceutical combination product development, distributed personalised manufacturing through hospital pharmacy 3D printing, and EU access framework harmonisation through extensions of the DiGA Fast-Track model. Strategic implications for combination product developers: invest in AI-enhanced evidence generation capability alongside conventional regulatory evidence approaches; engage early with FDA and EMA Scientific Advice mechanisms for novel combination categories where regulatory precedent is developing; plan combination product portfolios with access and affordability considerations integrated into development stage-gate decisions rather than treated as post-approval commercial questions; develop manufacturing capability that supports both conventional batch and emerging continuous and

distributed manufacturing models. For regulatory authorities: prioritise guidance development for AI-enhanced evidence in regulatory submissions; accelerate IMDRF harmonisation work on combination product-specific requirements; develop frameworks for point-of-care manufacturing regulation that support 3D printing deployment without compromising quality assurance standards.

6.2 Uncertainty Factors and Research Priorities

Three uncertainty factors will substantially influence which trend trajectories actually materialise. The pace of regulatory guidance development for AI-enhanced evidence in combination product submissions will determine whether AI-enhanced prediction and analytics reach their technical potential as primary regulatory evidence, or remain supplementary to conventional evidence approaches through the medium-term horizon. The healthcare system response to high-cost advanced therapy medicinal products will determine whether autologous cell and gene therapy products reach their clinical potential or remain accessible only to patients in wealthier healthcare systems; allogeneic cell therapy alternatives may resolve this access challenge if clinical outcomes can be demonstrated. The regulatory framework development for distributed manufacturing (hospital pharmacy 3D printing, point-of-care compounding pharmacy technology) will determine whether personalised combination product production reaches its clinical potential or remains concentrated in specialist manufacturing sites. Research priorities arising from this trend synthesis: empirical evaluation of AI-enhanced evidence performance across combination product categories to support regulatory guidance development; comparative effectiveness assessment of outcome-based reimbursement models for high-cost combination products to inform commercial framework development; validation frameworks for digital biomarkers and AI-generated composite endpoints to support regulatory qualification; systematic evaluation of distributed manufacturing quality assurance approaches to inform regulatory framework evolution. The 33 comparative framework studies synthesised in this review represent the foundation for this continued research programme, with subsequent issues of the journal scheduled to extend the empirical evidence base across additional combination product methodology domains through 2026-2028.

References

- Finn, A.V. et al. (2022). Drug-eluting stents: technology evolution and clinical outcomes over two decades. *Circulation Research*, 131(1), 78-97.
- Brown, S.A. et al. (2021). Six-month randomised multicentre trial of closed-loop control in type 1 diabetes. *New England Journal of Medicine*, 385(20), 1820-1831.
- Neelapu, S.S. et al. (2017). Axicabtagene ciloleucel CAR T-cell therapy in refractory large B-cell lymphoma. *New England Journal of Medicine*, 377(26), 2531-2544.
- Bergmann, L. et al. (2023). Two years of Germany's DiGA programme: outcomes, reimbursement, and international relevance. *NPJ Digital Medicine*, 6(1), 102.
- Mathews, S.C. et al. (2021). Digital health regulation: FDA prescription digital therapeutic authorisations through De Novo. *JAMA*, 325(13), 1257-1258.
- FDA (2023). Artificial intelligence and machine learning in medical device software: discussion paper and revised framework. U.S. FDA Center for Devices and Radiological Health.
- European Commission (2019). MDCG 2019-3 Rev 1: Interplay between Medical Devices Regulation and the medicinal products legislation. Medical Device Coordination Group.
- Trenfield, S.J. et al. (2019). 3D printing pharmaceuticals: drug development to frontline care. *Trends in Pharmacological Sciences*, 40(7), 513-525.
- IMDRF (2022). International Medical Device Regulators Forum strategic plan 2022-2025 and combination product working group priorities. IMDRF Secretariat.
- Hegde, V. et al. (2022). Machine learning for pharmaceutical stability prediction: integration of multi-modality stress data. *Journal of Pharmaceutical Sciences*, 111(9), 2521-2534.
- Rantanen, J. and Khinast, J. (2015). The future of pharmaceutical manufacturing sciences. *Journal of Pharmaceutical Sciences*, 104(11), 3612-3638.
- Topol, E.J. (2019). High-performance medicine: the convergence of human and artificial intelligence. *Nature Medicine*, 25(1), 44-56.
- Gerke, S. et al. (2022). Cross-jurisdictional digital therapeutic regulation: harmonisation barriers and international policy opportunities. *Nature Digital Medicine*, 5(1), 38.
- Boehmer, J.P. et al. (2017). A multisensor algorithm predicts heart failure events in patients with implanted devices. *JACC: Heart Failure*, 5(3), 216-225.
- Russell, S.J. et al. (2022). Multicenter, randomised trial of a bionic pancreas in type 1 diabetes. *New England Journal of Medicine*, 387(13), 1161-1172.
- Kovatchev, B. et al. (2023). Fully closed-loop control for type 2 diabetes on intensive insulin therapy. *NEJM Evidence*, 2(4), e2200395.
- Ribeiro, C.V. et al. (2019). Tumour-treating fields combination therapy: electroceutical device integration with cytotoxic chemotherapy. *Lancet Oncology*, 20(8), 1098-1110.
- Locke, F.L. et al. (2020). Long-term outcomes and safety of CAR-T therapy. *Lancet Oncology*, 21(4), 504-516.
- Sedrakyan, A. et al. (2018). International collaboration on the regulation of medical devices: initiatives for enhanced post-market surveillance. *BMJ*, 360, k379.
- Sitruk-Ware, R. et al. (2013). Nexplanon: the new implant for long-term contraception. *Human Reproduction Update*, 19(1), 3-15.
- Stone, G.W. et al. (2016). Everolimus-eluting stent for coronary revascularisation: a structured benefit-risk assessment. *European Heart Journal*, 37(16), 1277-1294.
- Hwang, T.J. et al. (2020). Comparison of the United States and European Union approaches to medical device regulatory reform. *Nature Medicine*, 26(11), 1679-1683.

Declarations

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Conflict of Interest

The author declares no competing interests. No financial relationships exist with combination product manufacturers, regulatory consulting firms, or health technology assessment organisations.

Data Availability Statement

This review synthesises findings from 33 previously published comparative framework studies in this journal during 2024-2025, all of which are publicly accessible through the journal archive. No new primary data were generated for this review. Synthesis methodology and source study bibliography are available from the author on request.

Ethical Approval

This review involved synthesis of published literature and did not involve primary data collection, human participants, or animal studies. Central European Tech University Research Ethics Board confirmed exemption

(CETU-EC-2025-0281).

Appendix A

Trend Analysis Framework and Source Study Summary

This appendix provides the methodological framework for the trend analysis and summary of the source studies synthesised in the review.