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Review

Discussion on the Regulatory Test of Artificial Intelligence-Enabled Medical Devices and Their Technical Potential in Tumor Immunity

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Abstract: The deep integration of AI and immunotherapy is reshaping the paradigm of cancer diagnosis and treatment. From biomarker discovery to personalized treatment, from adverse reaction warnings to empowering grassroots communities, despite bottlenecks such as data silos, algorithm transparency, and ethical controversies, the technical potential of AI has already begun to emerge. This paper examines the evolution of global AI medical device policies and product release trends over the past decade, identifying the issues and challenges posed by the current regulatory landscape, including: first, the structural imbalance between the regulatory system and the rate of technological innovation; second, the double-standardization dilemma between risk classification and clinical validation; and third, the ethical paradox of data governance and algorithmic transparency. The challenges faced include: first, Technology Fusion: AI at the Crossroads with Synthetic Biology and Nanotechnology. Second, Algorithm Transparency and Ethical Paradox. Third, In-Depth Application of Regulatory Technology. Fourth, Collaborative Innovation in Industrial Ecology. Based on this, this paper provides systematic recommendations for addressing the regulation of AI medical devices: first, Building a Dynamic Adaptive Technology Supervision System. Second, Perfecting the Full Life Cycle Clinical Evidence Chain. Third, Create an Open and Collaborative Industrial Innovation Ecosystem. Fourth, Deepen International Regulatory Coordination and Cooperation. Recommendations for the regulation of AI medical devices in the field of immunotherapy: First, Multi-Modality Imaging and Treatment Integrated Platform. Second, Intelligent Empowerment of Primary Care. Third, Global Collaboration and Data Sharing.

Keywords: AI Medical Devices; Regulatory Challenges; International Standards; Immunotherapy

1. Introduction

The fusion of artificial intelligence and medical devices is transforming the field of immunotherapy and cancer, demonstrating enormous potential over the past decade. However, with the heavier burden of cancer therapy and the growing importance of individual-based treatment, the demand to strengthen the regulation of artificial intelligence-enabled medical devices is becoming increasingly urgent. Although immunotherapy is revolutionary, patients always face challenges such as heterogeneity of responses, unpredictable immune-related adverse events (irAEs), and complex interactions of biomarkers. By utilizing the function for analyzing dynamic data, predicting models and supporting real-time decisions, AI can identify biomarkers by integrating multiple sets of data or predict side effects by analyzing electronic medical records. However, the rapid progress of technology such as generative AI and federated learning has run over the traditional regulatory framework for medical devices, which needs to

keep a balance with innovation and safety to adapt to the regulatory patterns. Regulatory agencies such as the FDA and the EMA have already attempted to make changes to address the challenges of AI, such as algorithm transparency, data privacy, and continuous learning systems. While the status of immunotherapy and AI in China is also complex due to systemic obstacles of developing AI medical devices, such as fragmented data ecosystems, limited interoperability of electronic health record systems, and inadequate ethical guidelines. Although significant progress was made in 2023 with the "Regulations on the Management of Artificial Intelligence Medical Devices (Draft for Public Comment)", which shows a positive attitude, the gap with IMDRF and WHO remains significant. The study reviews the progression of global AI medical device regulation, with a focus on the application of immunotherapy, the breakthrough of regulatory policy globally, and proposes strategies for the Chinese regulatory system to engage in innovation. China needs to meet the challenge over-across with global regulation for AI medical device, need to establish the advantage at late-move status, to establish dynamic levels supervise system, to push the application of the regulatory science, to participate in making global criterion, as to acquire the advantage in the competition of digital medicine all over the world. This research presents the current status of AI application in immunotherapy and attempts to propose potential solutions to address the complexities of ethics, technology, and regulation.

2. Artificial Intelligence Medical Device Development in the Past 10 Years

2013 International Medical Device Regulatory Authority Forum (International Medical Device Regulators Forum, IMDRF) released the milestone document "Software as a Medical Device: Key Definitions" [1], which is the first time that medical devices are independent software (Software as a Medical Device, SaMD) is included in the scope of medical device supervision. The object discussed in this document encompasses AI software, but explicitly excludes embedded systems that require hardware to operate [1]. Therefore, different countries or regions have adopted different regulatory concepts in practice, such as: Europe uses the concept of Medical Device Software (MDSW) to integrate various AI medical software [2]. At the same time, the US FDA supplements medical device independent software (SaMD) with Software In A Medical Device (SiMD) [3].

2.1. Technology Definitions and Conceptual Evolution

European AI technology has been applied in the medical field for some time. They define an AI system as "a system with intelligent behavior, which can take actions through analysis of the environment, has some autonomy, and can take specific action targets" [4]. It is an "intelligent system with autonomous decision-making ability" [4]. However, in fact, for most clinical AI technologies, an overemphasis on autonomy is not appropriate, because human supervision remain indispensable [5].

Unclear technical definitions pose many practical problems for regulation. For example, in 2018, Europe had a class of intelligent devices called AI watches, which were included in the artificial intelligence senior expert group according to the regulations at that time (High-level expert group, HLEG) [6]. Due to the lack of a clear standard definition, the concept of AI in the document version upgrade process, combined with different European countries using or in academic discussions of AI technology, derived from 69 different technical definitions [7], AI system supervision difficulties can be seen.

With the development of technology and the deepening of human cognition, it is believed that the definition of "AI system" should be more inclusive and practical, mainly when AI technology is used to guide production or evaluate clinical results for management, without being too rigid in defining software operation. In 2018, the European Commission first established HLEG, which is responsible for regulation, including AI systems [8]. In the same year, HLEG redefined AI systems as "functional modules in complex systems" [8], a change in technical definitions that highlighted the shift in regulatory thinking toward AI systems in a pragmatic direction.

The nature of the technology definition is to clarify the regulatory object and method; the vagueness of it will cause significant uncertainty of regulation. Former definition of AI system by European HLEG emphasized "intelligent behavior" and "independent decision" which reflect the concern about potential risk of complex system (for medical disaster by uncontrolled independent decision-making). In contrast, many auxiliary medical software without self decision ability was mistakenly embraced (for example: the image segmentation tool for only quantitative measurement). The broadening of definition caused resource misallocation, which limited the development of auxiliary medical software and risk system [4,6]. The practical challenges arise from the wide range of performance

spectra of AI systems, ranging from simple rule-based pattern recognition (such as early CADe) to complex deep learning models (such as predictive biomarker models), and potentially powerful AI systems that are still in development. At the early stage, IMDRF focused on SaMD, but the rapid popularization of SiMD exposed the limitations of the original definition. The US FDA proposed a definition of SiMD, aiming to fill the gap and consider the operational environment (whether relying on specific equipment) in regulatory considerations. In conclusion, the evolution of AI regulation has followed a trajectory that moves from abstract principles to practical applications.

2.2. Background and Requirements of Immunotherapy and AI Fusion Technology

Immunotherapy is a revolutionary approach to cancer treatment. It has achieved remarkable results in melanoma and non-small cell lung cancer by activating or enhancing the patient's immune system against tumors. However, its clinical application still faces many challenges: significant individual differences in efficacy, difficulty in predicting immune-related adverse reactions (irAEs), and complexity in biomarker detection. The application of artificial intelligence (AI) technology offers new solutions to address these challenges. AI's advantages in data integration, pattern recognition, and dynamic prediction enable it to optimize treatment plan design, improve biomarker detection efficiency, and facilitate real-time monitoring of treatment response, thereby pushing immunotherapy towards precision and intelligence [9,10].

In recent years, the global immunotherapy market has continued to expand, exceeding $50 billion by 2023. However, traditional clinical trial models struggle to cover 12%–15% of potential application scenarios for AI diagnostic systems, due to a lack of data drift. AI technology's dynamic learning capabilities and multimodal data analysis capabilities make it possible to break through this bottleneck. For example, generative AI (such as GPT-4 Medical Edition) can simulate the impact of different treatment options on the immune system, generate personalized treatment paths, and share data "available and invisible" across institutions through federated learning technology [10,11].

2.3. Laws, Regulations and Standards Construction

The AI Act was proposed in 2021 and is currently under parliamentary discussion [12]. AI embedded in medical devices must meet the requirements of both the AI Act and the Medical Device Regulation (MDR). The AI Act has not yet been adopted. The Scientific and Technological Options Assessment (STOA) of the European Parliament is advancing the agenda through scientific advisory services [13].

Organization for Economic Cooperation and The Organization for Economic Co-operation and Development (OECD) is a voluntary organization comprising 38 member states through non-statutory relations (WorldHealthOrganization, WHO) [14]. The OECD has developed multidimensional evaluation system that provides a new analytical framework for defining AI [13]. This multidimensional evaluation system, a "four-dimensional model" (technical characteristics, application scenarios, degree of autonomy, social impact) [14], that has been adopted by the World Health Organization (WHO) as a core dimension for evaluating medical AI [5].

Based on the GMDN term mapping and the policy text analysis of the three countries, policy has evolved from a single product to an algorithm and ultimately to synergy with clinical regulation [15]. For more information, refer to **Tables 1**, **2** and **3**.

Table 1. Classification Standardization Stage (2010-2016).

Region	Key Policies	GMDNMapping Node	Tumor Immune Influence
EU	MDD 93/42/EEC	AI diagnostic facilities → Code 65890	No distinction was made between AI and traditional devices
US	FDA UDI System Final Rule	SaMD → Code 70040	Immunotherapy AI is included in the high-risk category III
CN	"Medical Device Classification Catalogue" (2012 Edition)	AI auxiliary diagnosis	Tumor immune AI is managed as Class II

Table 2. Algorithm Supervision Stage (2017-2022).

Region	Milestone Events	EUR-Lex/NMPA gist [16]	Breakthrough
EU	MDR 2017/745	Article 123(3)(m)	Require the traceability of AI (such as CAR-T therapy AI)

Table 2. *Cont.*

Region	Milestone Events	EUR-Lex/NMPA gist [16]	Breakthrough
US	AI/ML SaMD Action Plan (2021)	21 CFR Part 860 Subpart C	Allow the "pre-certification" update of the PD-1 prediction model
CN	"Guiding Principles for the Registration Review of Artificial Intelligence Medical Devices" (2022)	NMPA Notice No. 14 of 2022	It pioneered the bias testing standard for tumor immune algorithms

Table 3. Ecological Synergy Stage (2023-present).

Region	New Regulatory Tools	New Terms of GMDN	Tumor Immunology Practice [17]
EU	EU AI Act (2024)	Code 88120: High-risk medical AI system	Mandatory clinical impact assessment of tumor immune AI
US	AI/ML SaMD Action Plan (2021)	Code 77000: Federal learning medical equipment	Cross-border tumor neoantigen database sharing framework
CN	"Guiding Principles for the Registration Review of Artificial Intelligence Medical Devices" (2022) [18]	Add: Dynamic Algorithm Quality Control	It is required that PD-L1 detection AI monitor the offset in real time

Compared with AI medical regulatory rules abroad, Chinese policy about immunotherapy has the following characteristics (**Table 4**).

Table 4. Chinese Policy About Artificial Intelligence Medical Devices Related to Immunotherapy.

Supervisor	Chinese Approach	International Benchmarking	Gap Analysis
Data diversity	Article 5.2 of the "Clinical Evaluation Guidelines for AI Medical Devices" (2023): Mandatory inclusion of tumor immunity data in the Asian population	IMDRF GSP-001 (2022): No explicit racial data requirements	Advantage: Filling the data gap of the Asian population
Penguin update	Dynamic Quality Control Specification: Half-year Revalidation (NMPA Notice No. 21, 2023)	Eu MDR Article 120: Version Freeze Mechanism FDA 21 CFR 820.30(g): Real-time updated filing system	Balance: Taking into account both safety and innovation
Multi-center validation	Limited to domestic tertiary hospitals (≥ 3)	IMDRF GSP-002 (2023): It is recommended to conduct cross-border multi-center verification (≥ 3 countries)	Weakness: Lack of a cross-border data mutual recognition mechanism

2.4. AI Medical Device System Supervision Key Changes and Immunotherapy Promotion

Changes in the definition of technology demonstrate a shift in regulatory thinking towards a pragmatic approach to AI systems. Currently, regulatory focus is shifting further from technology ontology regulation to applied risk management. For example, the US FDA allocates 50% of AI medical device approval resources to radiology diagnostic systems [18], reflecting regulatory considerations for balancing the high-risk characteristics and clinical value of AI medical devices.

The consensus is still developing, but there is no universally accepted version by regulatory agencies in various countries or regions, or major international organizations worldwide. In summary, the evolution of global AI medical device regulatory definitions presents three trends: First, technical descriptions shift from abstract features to specific algorithms (For example, ISO22989 specifies machine learning requirements) [19]; Second, risk classification is gradually linked to clinical impact (for example, the IMDRF four-category classification method) [20]; third, quality assessment extends from product performance to data lifecycle management (IEEE2801 standard) [21]. These changes have a direct impact on the compliance strategy of enterprises. For example, Siemens Medical has established a specialized AI model version control system to meet MDR requirements [22].

Immunotherapy is categorized as "High Risk" in the EU AI Act, which requires developers to submit and algorithm interpretability report and long-term safety data. The FDA proposed that "AI medical equipment accelerates the approval process", which enables immunotherapy to launch based on real-world evidence rapidly, but with continuous supervised data. AI Medical Device Data is proposed by the ISO/IEC Joint Technical Committee, which

standardized the process of data collection, model training, and clinical identification. While WHO emphasizes the importance of "human oversight" in Medical Ethics Guidelines [14,23].

2.5. AI Medical Device Supervision Thinking and Immunotherapy System Practice in China

In 2014, the International Medical Device Regulators Forum (IMDRF) guidelines on SaMD identified two main aspects of risk: the functionality of the software and the severity of the disease [20]. If SaMD is used for the diagnosis and treatment of serious or critical illness, it should be classified as a high-risk group (Classification III and IV in the document) [24]. Chinese regulatory authorities have issues special guidance, noting that the low maturity of artificial intelligence systems in medical applications means that their safety and effectiveness have not been fully established; thereby, they should be classified as Class III medical devices (i.e., medical devices implanted in the human body, used to support and sustain life, and whose safety and effectiveness must be strictly controlled) [25]. At the same time, Chinese regulatory authorities believe that if it is not used to assist medical decision-making, but only for data processing or measurement to provide clinical reference information, it can also be managed as Class II medical devices. This is similar to the current UK regulatory mechanism, known as the Airlock Classification Rule, which classifies SaMDs with an unclear risk profile as Class III [26].

The "Administrative Measures for Artificial Intelligence Medical Devices (Draft for Public Comment)" released in 2023 stipulates that AI-enabled immunotherapy should test clinical safety and efficacy. NMPA incorporates AI-enabled diagnosis into the medical insurance system in 2024, which accelerated the commercialized speed of the biomarker system [14,27]. In addition, the draft Personal Health Information Protection Act enhanced the protection of personal information, including medical data, to ensure the safety of patients during treatment. A "three-dimensional regulatory matrix" is proposed in the policy, including three dimensions: a technical dimension (algorithm maturity rating), an application dimension (clinical impact index assessment), and a data dimension (federal learning regulatory interface) [11,27].

3. Market Situation of Artificial Intelligence Medical Devices in Recent 10 Years

3.1. Basic Situation of AI Medical Device Marketing in Recent 10 Years [28]

The first IMDRF SaMD product received FDA approval in 2012; since then, the number of such products approved has grown from 1 to 581 from 2012 to 2021, a CAGR of 202.7% (**Figure 1**). The first AI- or machine learning-based SaMD product received FDA approval in 2016, and the number grew to 37 by 2021. AI or machine learning-based SaMDs currently account for 22% of FDA-approved SaMDs.

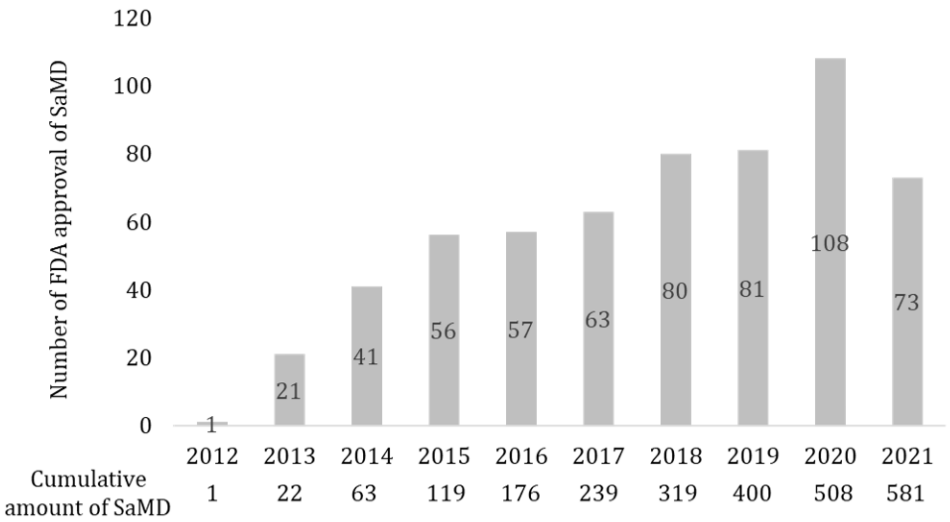

Figure 1. Number of FDA approved SaMD.

Source: https://www.jmir.org/2023/1/e47505.

Radiology medical software is the most frequent product category in SaMD (n = 452, 78%), followed by cardiovascular (n = 54, 9%), neurology (n = 26, 4%), ophthalmology (n = 15, 3%), and dentistry (n = 10, 2%). Among product categories, medical equipment, medical devices and software account for 66% (n = 385). The majority of radiology SaMD is used for image processing and analysis (n = 378).

At the enterprise level, large companies such as Siemens, General Electric (GE), and Philips reported the most SaMD devices (n = 237, 40.8%), followed by small and medium-sized companies (n = 215, 37%), most of which were established after 2012. The data show that companies tend to develop peripheral products for SaMD devices to strengthen their competitive edge in the market, as seen with Siemens, GE, and Philips in medical imaging.

Multiple mergers and acquisitions occurred in the past, especially in the past 3 years, on the market side. Forty-three companies had acquired 263 startups from 2012; 21 deals among them took place in the past 3 years. Americans (n = 262, 45%) declared the most in the surveyed country, followed by Germans (n = 71, 12%), Koreans (n = 32, 5.5%), and the Netherlands (n = 27, 4.6%). America has absolute leadership in the yield of SaMD. The distinction between America and Germany is where the most innovations come from. In America, it comes from startups and in Germany from public companies. This phenomenon indicates the importance of the entrepreneurial ecosystem in America.

3.2. Approval for Listing of AI SaMD in China

Although China Artificial Intelligence Medical Device (AISaMD) has made breakthrough progress in regulatory approval in recent years, the "Fractional Coronary Flow Reserve Calculation Software" developed by Beijing Kunlun Medical Cloud Technology Co., Ltd. approved in January 2020 is the first product in China to obtain the registration certificate for Class III artificial intelligence medical device. In August 2022, the fundus image-assisted diagnosis software launched by the Kangfu subsidiary of Baidu won the approval of the State Drug Administration (National Medical Products Administration, NMPA), became the first Class III certificate for multi-disease AI medical devices in China. However, the overall industry still faces systematic challenges, mainly reflected in the limited variety and quantity of products. By the end of September 2023, there were 53 Class III deep learning independent software in China [29]. In terms of distribution, CT image software, X-ray image software, and fundus image software have high product concentration, while MR image software, microscope image software, ultrasound image software, and pathological image software are still gaps [30]. Policy supervision restricts the iteration of technology and industrial-scale processes, so it is necessary to improve relevant laws and regulations as soon as possible to activate the innovation ability of AI medical devices under standardized conditions.

3.3. Potential Reference Scenarios of Artificial Intelligence Medical Devices in Immunotherapy

3.3.1. Biomarker Screening and Efficacy Prediction

AI can identify key biomarkers related to immunotherapy response by integrating genomic, transcriptome, proteome, and other multi-omics data. For example, ChatZOC, a large ophthalmology model jointly developed by the Zhongshan Eye Center of Sun Yat-sen University and Huawei, enables disease stratification based on multimodal data, and its technical path can be applied to the immunotherapy field. Similarly, RuiPath, developed by Ruijin Hospital of Shanghai Jiao Tong University and Huawei, optimizes patient enrollment criteria by analyzing millions of pathological section data, thereby increasing clinical trial efficiency by 40% [11,26]. In addition, AI can also evaluate treatment response in real-time by analyzing dynamic changes in circulating tumor DNA (ctDNA) to avoid ineffective treatments. For example, the Ding Health Large Model of the Second People's Hospital of Guangdong Province has developed an active early warning framework for chronic disease risk, which can be adapted for toxicity monitoring in immunotherapy [11].

3.3.2. Individualized Treatment Plan Design

AI algorithms can identify patients (such as through HLA typing and tumor mutation load) and recommended optimal drug combinations and doses. Huawei and Shandong University Qilu Hospital jointly developed the "Qilu· Heart Acute Chest Pain Large Model", which achieves accurate stratification through multimodal data fusion. Similar models can be extended to immunotherapy combination scenarios. In the future, generative AI may simulate the impact of different treatment regimens on the immune system and generate personalized treatment paths [11]. For

example, Siemens Medical's "Medical Digital Man" technology provides visual support for treatment decisions by constructing virtual physiological models of patients and dynamically simulating tumor microenvironments [31].

3.3.3. Early Warning and Management of Immune-Related Adverse Reactions (irAEs)

AI enables the early identification of patients at high risk for irAEs by analyzing electronic health records (EHRs), imaging, and laboratory data. For example, BD's HemoSphere Alta™ blood flow monitoring platform uses AI to predict hypotension events. Its algorithms reduce the depth and duration of hypotension events, a technology framework that can be migrated to immunotherapy toxicity monitoring [32]. Additionally, natural language processing (NLP) technology automatically parses patient complaints to help physicians quickly identify the type of adverse reaction. The Shengteng AI computing platform, developed by Huawei in cooperation with medical institutions, has supported accelerated data analysis of multiple immunotherapy clinical trials [11].

3.3.4. R & D Support for Novel Immunotherapy Technologies

The application of AI in drug discovery has been extended to the field of immunotherapy. For example, the structure of immune checkpoint inhibitors is optimized through virtual screening technology, or novel CAR-T cell targets are designed. The AIEgen bacterial hybrid bionic robot (EcN@INX-2) developed by the Guangzhou Medical University team combines phototherapy and immune activation functions, and optimizing the synergy between photosensitizers and probiotic carriers through AI algorithms, and significantly enhances the anti-tumor immune response [33].

4. Global Regulatory Challenges Faced by Artificial Intelligence Medical Devices and China'S Response Strategies

4.1. The current global regulatory situation of artificial intelligence medical devices

Regulatory strategy implementation framework (**Table 5**):

(1) Example for Technical Validation: The breakthrough certification of the global first AI diagnosis system Paige Prostate established the cross-validation process about "Algorithm - Immunohistochemical Results", solving the problem of heterogeneity of the tumor microenvironment. The certification requires continuous submission of pathological section data of prostate cancer from 127 hospitals across 6 countries.

(2) Example for Ecosystem Governance: The regulation of Phillip's AI tumor platform under EU IVDR, which incorporates a "dynamic data pricing model" to design the local market for immunotherapy data elements. To establish medical data trust, the platform allows the hospital to retain ownership of the data, and developers can only access the data through the API, with payment.

(3) Example for International Collaboration: The US-Japan co-developed OncoAssist—a predictive AI for PD-1 response—established an immune-oncology genomic database across ethnic groups to minimize differences in TMB threshold values between US and Asian populations. The development adopted the unified framework of IMDRF's SaMD Quality Management System.

Table 5. Implementation Framework for Regulatory Strategies for Artificial Intelligence Medical Devices Related to Immunotherapy.

Supervisor	Core Strategy	Implementary Mechanism	Tumor Immunology Application Scenarios
Technical Validation	Dynamic Certification	1) Establish a dynamic update and filing mechanism for AI algorithms 2) Introduce federated learning sandbox testing for multi-center data collaboration 3) Develop verification tools for tumor immune-specific algorithms (such as a tumor microenvironment simulation verification platform)	1) Iterative regulation of the response prediction model for PD-1/PD-L1 inhibitors 2) Preclinical validation of AI screening algorithms for tumor neoantigens

Table 5. *Cont.*

Supervisor	Core Strategy	Implementary Mechanism	Tumor Immunology Application Scenarios
Ecosystem Governance	Lifecycle Collaboration	1) Build a data trust platform of "AI developers - medical institutions - pharmaceutical companies - regulatory authorities" 2) Develop the annotation standards for tumor immune data (such as RECIST 1.1+AI Enhanced Edition) 3) Establish an AI medical malpractice accountability flowchart	1) The multi-party collaboration of the AI-driven toxicity early warning system in CAR-T therapy 2) Cross-institutional data sharing governance of tumor vaccines and AI individualized drug delivery systems
International collaboration	Standard mutual recognition and crisis response	1) Join the IMDRF AIWG working group to promote the internationalization of Chinese standards 2) Establish the Asia-Pacific Tumor Immunology AI Regulatory Alliance (APAC-OncoAI) 3) Establish a cross-border traceability mechanism for algorithmic biases	1) Algorithm offset correction in cross-border multicenter clinical studies (such as the difference in TMB threshold between Asian and European and American populations) 2) Global AI Surveillance Network for Tumor Immune Resistance

4.1.1. Structural Imbalance between Regulatory System and Technological Innovation Rate

The technology iteration cycle of AI medical devices has been shortened to 6-12 months, while the average update cycle of traditional medical device regulatory frameworks is as long as 3-5 years. Take deep learning algorithms as an example, their parameter scale has expanded from millions in 2016 (such as U-Net) to tens of billions in 2023 (e.g. Med-PaLM2). However, existing regulatory standards are still based on static software characteristics. The IMDRF survey shows that 78% of AI enterprises believe current regulations are not suitable for continuous learning systems (CLS) [29]. This lag is particularly prominent in multinational regulation: the EU MDR requires locked versions of algorithms to be certified, whereas the FDA allows some CLS to update autonomously within preset control ranges, resulting in companies developing differentiated products for different markets [32].

4.1.2. Double-Standardization Dilemma between Risk Classification and Clinical Validation

There are significant differences in risk classification criteria across major regulatory regimes worldwide (**Table 6**). For example, the European Union ranks risks based on the impact of algorithm outputs on diagnostic decisions (MDCG2019-11), while the FDA adopts a two-dimensional model of "software function + disease severity" (IMDRFN12) [30]. This difference leads to a risk classification bias of 2–3 levels for the same product in different markets, resulting in an average 27% increase in the enterprise's compliance cost [34]. At the clinical validation level, it is difficult to assess the long tail effect of AI systems in existing randomized controlled trial (RCT) models. Studies have shown that traditional clinical trials cover only 12–15% of potential application scenarios for AI diagnostic systems [35] and lack continuous monitoring mechanisms for data drift.

Table 6. Comparison of Core Dimensions of Risk Classification in the United States and Europe.

	EU MDR (MDCG2019-11)	FDA (IMDRF N12)
core concept	the contribution of ultimate medical decision with AI output	software function + disease progression
classic high-risk scene	AI outcome is the main evidence about doctor decision	AI for diagnosis/treatment of high lethality disease
Practical Difference Cases	The immunological microenvironment quantification tool may be classified as Class I/IIa.	If the tool is associated with fatal diseases (such as lung cancer), it should be classified as Class II.

For the same immunotherapy prediction AI (suppose it is used for predicting the response of an NSCLC patient with PD-1 therapy), according to MDR, if the doctor makes a prescription based on its output (high-risk decision), the risk level may be classified into IIb or III. If the function definition is "Diagnostic" and the indication is lung cancer (a disease with a high lethality rate), it also belongs to class III. However, the outcome seems the same, if the output of the software is only quantitative values of immune microenvironment characteristics which is not enough for a physician's prescription decision. It may be classified as class I or IIa (low risk), while the FDA also needs to consider the indication. The rules cause global compliance obstacles.

4.1.3. The Ethical Paradox of Data Governance and Algorithmic Transparency

AI medical devices rely on massive medical data facing triple contradiction: First, the conflict between data acquisition requirements and privacy protection, GDPR requires data anonymization, but medical image de-identification may lead to the loss of key features (for example, the location information of skin lesions) [36]; Second, the contradiction between algorithm interpretability requirements and trade secret protection, FDA requires disclosure of core algorithm logic, but the patent disclosure rate of enterprises is less than 40% [35]; Third, the contradiction between data sovereignty and cross-border circulation, the interoperability rate of Sino-US electronic health records (EHR) system is only 8.3%, which seriously restricts transnational multicenter research [34].

4.2. Global Regulatory Challenges for AI Medical Devices

4.2.1. Technology Fusion: AI at the Crossroads with Synthetic Biology and Nanotechnology

Artificial Intelligence may guide the design of new immune molecules or enhance the efficiency of drug delivery by nano-carrier in the future. For example, the incorporation of AI and bacteria carrier shows the potential capacity in "living AI drug" [32]. In addition, the combination of wearable devices and AI may make the supervision of immunotherapy at home a reality, such as smart bracelets that predict irAEs6 by analyzing heart rate variability (HRV).

4.2.2. Algorithm Transparency and Ethical Paradox

The generalization ability of AI models relies on diverse datasets; however, data sovereignty and cross-border circulation are often contradictory. For example, the GDPR requires data anonymization, but the de-identification of medical images may lead to the loss of key features [28]. CONSORT-AI and SPIRIT-AI guidelines emphasize that clinical trials should disclose their algorithm logic and data sources; however, corporate patent disclosure rates are less than 40%, and a balance needs to be struck between trade secrets and regulatory transparency [28].

4.2.3. In-Depth Application of Regulatory Technology

Blockchain technology can be utilized for version control and data traceability in immunotherapy AI systems, such as Siemens Medical's "algorithmic change blockchain storage system". Regulators may introduce AI review tools to automatically detect compliance of clinical trial data [11,32].

4.2.4. Collaborative Innovation in Industrial Ecology

Huawei proposes the "three unification" strategy (unified technical architecture, data standards, interface specifications), promoting the deep integration of medical AI. Medical institutions need to build AI-native capabilities, combine models, data, and domain knowledge, and achieve continuous learning and evolution [11]. The State Food and Drug Administration has established a "regulatory sandbox" mechanism to provide an 18-month testing period for emerging fields, such as digital therapy (DTx), to accelerate technology iteration.

4.3. Systematic Recommendations for China to Meet the Regulatory Challenges of Artificial Intelligence Medical Devices

4.3.1. Building a Dynamic Adaptive Technology Supervision System

It is suggested to establish "three-dimensional supervision matrix": in the technical dimension, introduce algorithm maturity classification (refer to NMPA Guidelines for Technical Review of Artificial Intelligence Assisted Software), implement dynamic monitoring for systems above L3 level (conditional autonomy); in the application dimension, establish clinical impact index evaluation model to quantify the impact weight of AI decision on diagnosis and treatment path; in the data dimension, develop federal learning supervision interface to realize controllable sharing of data "available and invisible." The FDAPre-Cert 2.0 program can serve as a model to establish a fast-track approval channel for enterprises certified as "digital centers of excellence" and to require the implementation of a blockchain certificate system for algorithm changes [33].

4.3.2. Perfecting the Full Life Cycle Clinical Evidence Chain

A three-stage evidence system should be constructed: pre-market stage, development of validation toolkit based on characteristics of China population (for example, liver image AI test set with high incidence of hepatitis B); in the use stage, establish a continuous collection mechanism of real-world data, and require enterprises to submit data drift monitoring reports every quarter; in the post-marketing stage, implement anti-sample stress test to evaluate the model failure boundary. Reference can be made to EU MDRAnexXIV requirements to clarify that algorithm retraining must utilize certified data cleansing tools and establish manual review nodes in critical clinical scenarios, such as emergency triage [36].

4.3.3. Create an Open and Collaborative Industrial Innovation Ecosystem

It is suggested to implement the strategy of "two-wheel drive": at the basic level, set up a national medical AI innovation center, focusing on overcoming multi-modal data fusion, small sample learning and other "neck" technologies; at the application level, implement the supervision sandbox mechanism to treat digital therapy (Digital Therapeutics, DTx) and other emerging fields will be given an 18-month test period. At the same time, a "three horizontal and three vertical" collaborative network will be established, integrating medical institutions, AI enterprises, and cloud service providers horizontally, and connecting provincial, city, and county-level medical data platforms vertically. For example, Shenzhen has piloted the "Bay Area Medical AI Collaborative Platform" to achieve standardized data access for 67 hospitals and support rapid iteration of domestic AI devices [37].

4.3.4. Deepen International Regulatory Coordination and Cooperation

It is necessary to focus on three aspects of work: first, leading the formulation of AI device standards with traditional Chinese medicine characteristics (for example, tongue diagnosis image analysis system), output China scheme through IMDRF and other channels; secondly, establish cross-border mutual recognition "white list" to open ASEAN market fast channel for Class II AI devices certified by NMPA; thirdly, participate in the revision of WHO artificial intelligence ethical governance framework, and promote the inclusion of "human supervision right" into global standards. Currently, China holds technical advantages in the field of medical natural language processing, and it is necessary to expedite the development of international standards for Chinese medical text analysis [38].

4.4. Systematic Suggestions for China to Meet the Regulatory Challenges of Artificial Intelligence Medical Devices in the Field of Immunotherapy in the Future

4.4.1. Multi-Modality Imaging and Treatment Integrated Platform

DeepwiseMetAIX, a multi-modal intelligent image large model capability platform released by Shenrui Medical, integrates multi-modal data such as radiation, ultrasound, and nuclear medicine to reconstruct intelligent boundaries of medical images and realize a full link connection from examination reservation to scientific research transformation. The platform seamlessly integrates diagnosis and treatment links through AI algorithms, improving diagnosis efficiency by 30% [32]. Siemens Medical's "Medical Digital Man" technology dynamically simulates the tumor microenvironment through virtual physiological models to provide visual decision support for immunotherapy [32].

4.4.2. Intelligent Empowerment of Primary Care

AI technology is driving down the resources for immunotherapy. For example, the ChatZOC ophthalmology model enables primary patients to complete a preliminary screening remotely through a mobile phone preconsultation system, and similar models have been extended to immunotherapy indication evaluation. Haier Biomedical's smart vaccine platform achieves full process traceability through IoT technology, and its data management experience provides a reference for cold chain monitoring of immunotherapy drugs [11,32].

4.4.3. Global Collaboration and Data Sharing

The interoperability rate of China-US electronic health records (EHR) systems is less than 10%. It is urgent to establish a multinational data alliance. The State Food and Drug Administration proposes to promote global regulatory coordination, support enterprises in participating in the formulation of international standards (such as

the IMDRF and GHWP), and expand the scope of medical device export sales certification. Huawei Shengteng Cloud collaborates with 62 leading hospitals worldwide to develop a "computing power + data + application" trinity model, helping to globalize AI technology [11].

5. Conclusion and Prospects

We come up with three ways for: First is to establish dynamic risk levels for clinical effect such as "Three-dimensional supervision matrix" which introduces algorithm maturity level classification from technological site, establishes index model for evaluating clinical efficacy and develops a regulatory interface for federated learning based on data dimension [39]; Second is to collect the evidence chain throughout the entire life cycle from pre-clinical to NDA, including character group of Chinese people in clinical trial, rules for continuous data collecting after prescription in real word and post-launch sample stress testing [35]. Third is to standardize the criteria of ethics and technology for global cooperation, as well as to establish a traditional Chinese medical AI device standard, or to make a "white list" for cross-border mutual recognition and to participate in the revision of the WHO's artificial intelligence ethics governance framework [40]. The transformation from "product supervision" to "ecological governance" of global AI medical device supervision reflects both the change in risk control from a single product to a technology stack and the extension of evaluation from clinical efficacy to health economics.

For China, it is necessary to meet the challenge of transnational regulatory coordination (for example, the difference between Chinese and American electronic medical record standards leads to difficulties in mutual recognition of data) [39], and it is also necessary to capitalize on the opportunity of a latecomer advantage (for example, the federal learning platform supported by digital new infrastructure) [41]. It is suggested to break through in three aspects: first, establish a dynamic hierarchical supervision system and implement "algorithm black box" review for L4-level autonomous diagnosis system [42]; second, promote the application of regulatory technology (RegTech) and develop AI review auxiliary system to improve efficiency [42]; Third, participate in the formulation of international standards and output China solutions in the advantageous fields of medical natural language processing and multimodal fusion [43].

Future research may focus on the impact of generative AI on medical device boundaries (e.g., ChatGPT-enabled diagnostic systems) [44], regulatory paradigm innovation for brain-computer interface devices [45], and the construction of a compliance framework for meta-universe medical scenarios [46]. Only by establishing a proactive regulatory system can we take a strategic lead in the global digital health competition.

Author Contributions

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Conflicts of Interest

The authors declare that they have no conflict of interest.

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