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EVH Regulatory Preparedness Strategy

Anticipation and Preparation for the next pandemic

Executive Summary

The European Vaccines Hub (EVH) serves as a coordinative platform for the development of pandemic vaccines and monoclonal antibodies (mAb). Its ambition is to support vaccine and antibody development across all stages, seamlessly leading to large-scale manufacturing and marketing authorisation. To fulfill this objective, the EVH will follow its Vaccines Readiness Plan (VRP), which covers the relevant aspects from pathogen selection to pre-pandemic vaccine development and stress testing of the network. This document specifically addresses the EVH strategy for anticipation and preparation for challenges that might impede product development, manufacturing and marketing authorisation in a pandemic.

In emergency outbreak situations, the EVH will take a central role in enabling rapid access to data and coordination of fast-track authorisation pathways already established by EMA, including rolling submissions and adaptive clinical trial designs. Moreover, EVH will interact with regional authorities overseeing production sites. The following major action fields for EVH preparatory regulatory activities have been identified:

1. **Warm-base and preparedness concepts throughout the EVH.** EVH partners will seek early engagement with the EMA to obtain regulatory alignment on critical development and manufacturing processes and approval of selected pre-pandemic medicinal products. For example, EVH-supported prototype candidates for epidemic and pandemic vaccines will be developed through completion of phase II clinical trials followed by submission of a regulatory dossier to confirm the formal acceptability of the strategy for accelerated product development in an epidemic or pandemic situation. These actions will further include qualification and validation of assays to be used for preclinical and clinical testing, clinical trial protocols, manufacturing processes, and qualification of quality control methods for batch release testing. In particular, the EVH will further engage in progressing the regulatory positioning of platform technologies for rapid pandemic vaccine development and manufacturing in public health crises.

2. **Measures to accelerate vaccine development and manufacturing.** The EVH will evaluate new approaches to speed up individual development phases and the seamless transition through all development stages to marketing authorisation. To this end, the EVH will leverage the application of AI and machine learning tools, will attempt to prepare CHIM studies if suitable for candidate vaccine products and pathogens of pandemic relevance, develop innovative in vitro models for preclinical and clinical testing, and develop platform-, cohort- and epidemiology-based innovative clinical trial designs.

To achieve these objectives, the EVH developed a dual approach to tackle the predictable regulatory hurdles, which relies on 1) support for individual product candidates and preparedness activities within and in cooperation with the EVH, and 2) overarching activities that contribute to the identification of unresolved general regulatory issues, promote global harmonisation of regulatory pathways and/or data provision facilitating regulatory decision-making in a pandemic scenario. The EVH regulatory team will function as a contact point for EMA and national competent authorities regulating medicines and their production to proactively communicate regulatory needs and support the regulatory path to approval of EVH product candidates.

Product and preparedness support: The EVH regulatory team will provide comprehensive guidance during the development of medicinal product candidates as well as preparedness activities requiring pre-approval strategies such as standardised clinical trial protocols or CMC files for pandemic readiness. It will address regulatory requirements in early development and pandemic preparedness to increase efficiency and ensure regulatory acceptability through provision of documentation, safety standards and GxP compliance.

Strategic support of regulatory preparedness: The EVH regulatory team intends to become an important driver of pandemic-related topics of regulatory relevance. It will shape the discussion and drive regulatory innovation through think tanks and white papers in key areas where identification of regulatory gaps and regulatory harmonisation are needed. These activities will focus on critical aspects of pandemic preparedness such as platform-based vaccine regulation, innovative clinical development concepts during epidemic and pandemic crises, crisis-ready manufacturing concepts, and alternative administration routes.

Regulatory research concept: The EVH will identify areas where regulatory decision-making is hampered by lack of data and uncertainties that affect pandemic preparedness strategies in vaccine development and manufacturing. Based on these analyses, the EVH will initiate research projects to obtain data and analyses that facilitate regulatory decision-making in these areas.

Communication and education: The EVH will proactively reach out to relevant stakeholders and partners within and outside of EVH to establish a cross-sectorial expert network to provide a platform for exchange on pandemic-relevant regulatory topics. It will further contribute to developing and maintaining regulatory-relevant expertise through educational and training activities. Transparent communication of EVH activities and developments will be implemented to build public trust and counteract misinformation.

Detailed Description of Anticipatory Measures Planned to Achieve Regulatory Preparedness in the European Vaccines Hub

I. Background

The European Vaccines Hub (EVH) serves as a coordinating platform for the development of pandemic vaccines and monoclonal antibodies (mAbs). Its mission is to support vaccine and antibody development across all stages, from preclinical research to large-scale manufacturing and marketing authorisation, ensuring a seamless transition from discovery to deployment.

All EVH activities are designed to strengthen Europe's capacity to move rapidly from pathogen identification to vaccine authorisation during a public health emergency (PHE). This requires a preparedness model that integrates scientific readiness, regulatory alignment, and manufacturing capacity in a coordinated and predictable manner.

The COVID-19 pandemic demonstrated that rapid vaccine and mAb development is feasible when enabling technologies, clinical and preclinical evidence, manufacturing infrastructure, and regulatory pathways are established, harmonised, and maintained in a state of readiness before an outbreak - a concept known as "warm basing." This experience also highlights the critical need for sustained investment in platform technologies, resilient manufacturing capacities, streamlined regulatory frameworks, real-time data sharing, and reliable public-private partnerships.

Building on these lessons, the EVH will embed critical capabilities into routine preparedness, ensuring they remain operational and scalable to enable a faster, more coordinated, and more effective response to future emerging infectious disease threats. To operationalise this objective, the EVH will develop and implement the Vaccines Readiness Plan (VRP), a comprehensive framework encompassing pathogen prioritisation, pre-pandemic development of prototype vaccines, warm-base manufacturing and regulatory readiness, rapidly available clinical trial capacity and end-to-end stress testing of Europe's vaccine development and deployment systems.

The regulatory preparedness strategy presented here serves as a detailed operational complement to the VRP framework, translating its high-level objectives into concrete regulatory pathways, evidence requirements, and implementation mechanisms. It specifically addresses how the EVH will anticipate and mitigate regulatory challenges that could otherwise delay product development, manufacturing, or marketing authorisation during a PHE. During emergencies, the EVH will leverage knowledge and processes established during pre-pandemic preparedness phases. By proactively strengthening regulatory readiness and fostering early engagement with regulatory authorities, the strategy aims to accelerate the availability of safe, efficacious, and high-quality vaccines and mAbs when they are most needed. In a pandemic scenario, the EVH will serve as a central coordinating point for vaccine and monoclonal antibody (mAb) development initiatives across Europe. It will accelerate development by leveraging established pipelines, enabling rapid data exchange, and implementing harmonised protocols for fast-track authorisation pathways (e.g., rolling submissions and adaptive trial designs). Through direct coordination with regional and European regulatory authorities, the EVH will streamline all stages of the

development process - from preclinical research through to market authorisation and mass manufacturing - positioning itself as the central interlocutor for licensure and deployment.

Two strategic objectives guide the EVH's preparatory regulatory activities:

1. **EVH Warm-Base Support & Preparedness Concepts:** Sustaining readiness across the EVH development pipeline through proactive warm-basing strategies and implementing novel methodologies and preparedness concepts.
2. **Regulatory Research & Acceleration for Europe:** Advancing regulatory science and targeted initiatives to accelerate vaccine development and manufacturing, both within the European Union and in international partnerships.

These objectives, supported by a structured communication strategy, form the cornerstone of the EVH regulatory strategy. The first action field focuses on internal capacity building to establish a state of readiness within the EVH that can be rapidly mobilised during an outbreak. This includes direct support for new technologies and tailored measures for each development phase to ensure timely implementation and seamless progression for both internal and external product candidates. These support measures will be continuously refined and expanded based on operational experience and emerging scientific insights.

The second objective centres on advancing European and global regulatory preparedness through targeted regulatory research designed to acquire the data required for informed decision-making. A key priority is determining which existing data can be leveraged to establish the knowledge needed for accelerated development and manufacturing. Complementing this, the EVH will generate missing evidence, address predictability and barriers in the development pathway, and evaluate innovative approaches for regulatory processes - including AI-enabled tools, controlled human infection models, novel in vitro systems, and platform-, cohort-, and epidemiology-based clinical trial designs. Together, these efforts should enable faster, more predictable regulatory decisions and streamline the transition from preclinical research to marketing authorisation.

The EVH's regulatory preparedness strategy is designed to ensure that Europe can progress from pathogen identification to vaccine authorisation within significantly expedited timelines. This requires a coordinated approach that integrates scientific readiness, regulatory alignment, and manufacturing feasibility into a single, predictable framework. Accordingly, the EVH regulatory team will serve as a central facilitator and coordinator, enabling early engagement with regulatory authorities, supporting platform-based development strategies, and ensuring that critical regulatory prerequisites - such as data requirements, documentation readiness, and submission pathways - are established proactively, well before a crisis emerges.

To achieve these objectives, the EVH regulatory work program is structured around five key action fields that align with the EVH's strategic framework:

1. Warm-Base Preparedness Concepts
2. Regulatory Product and Pipeline Support
3. Acceleration of Developments through Implementation of New Technologies & Methodologies
4. Advancing European Pandemic Preparedness through Regulatory Intelligence, Methodology & Research
5. Education, Training & Communication

II. EVH Support & Preparedness

The EVH brings together leading academic developers and European vaccine research institutions to develop an integrated and connected European development pipeline. By leveraging Europe's combined potential as an integrated network, EVH can advance vaccines and monoclonal antibodies far more rapidly than isolated efforts would allow.

A core component for facilitating rapid development is clear, structured regulatory support from the first to the last step of the pipeline. This chapter outlines how EVH's regulatory activities support product and pipeline development to facilitate rapid and secure product advancement during a public health emergency.

a. Warm-Base Concepts

Warm-basing means keeping regulatory, scientific, and manufacturing readiness in place before a crisis hits. Instead of waiting for an outbreak to define data requirements, clinical trial designs, or manufacturing standards, the EVH maintains these elements in a state of operational readiness through ongoing collaboration projects. This involves continuous regulatory dialogue, pre-qualifying standardised platform-specific CMC documentation, and quality control assays, as well as keeping manufacturing pathways qualified and auditable. The practical goal is obvious: once a PHE pathogen is identified, development is redirected, not initiated. By maintaining the foundations, warm-basing turns product development into a predictable, repeatable process that reduces development time without compromising safety or quality in times of crisis.

These warm-base activities sit at the core of the EVH's regulatory work and form the foundation for continuously refining the processes across the EVH product development line. Key steps include clarifying baseline CMC data requirements for platform technologies, defining pre-clinical data expectations, establishing suitable preclinical models, developing criteria for first-in-human studies, method qualification for preclinical and clinical immunogenicity testing, and developing standardised templates for clinical trial protocols. Collectively, continuously meeting and updating these regulatory requirements and integrating them into the EVH's warm-base framework is key for preparedness.

To expedite clinical development and early access to vaccine and mAb candidates with high technological readiness level, three major readiness measures are required: (1) readiness for technology transfer and manufacturing of clinical lots, (2) readiness to produce vaccine and mAb candidates that have reached Phase 2 or received a conditional marketing authorisation, and (3) readiness for upscaling to mass manufacturing. To achieve these objectives, the EVH will contribute to establishing warm-base concepts in manufacturing and provide regulatory support to secure readiness. This includes pre-qualifying GMP facilities, securing supply chains for and qualification of critical raw materials, validating scale-up strategies in advance, and ensuring that manufacturing sites meet regulatory requirements. These measures ensure that production can begin quickly and reliably once a new vaccine or monoclonal antibody candidate is selected for emergency development.

For CMC-related tasks, the goal is to support the implementation of masterfile documents, such as pathogen-agnostic manufacturing process descriptions and qualified and validated QA/QC methods for assays used in quality control, batch release, and stability testing, and to leverage the proposed introduction of the platform technology concept into the EU pharmaceutical legislation. This work can be initiated and tested within the EU-FAB and ZEPAI manufacturer networks, which maintain manufacturing capacity and GMP readiness through pandemic preparedness contracts. The EVH will align the content of these master documents with the EMA, its ETF and national and regional authorities through structured preparatory exchanges and formal Scientific Advice procedures.

To ensure effective pandemic responsiveness, warm-base concepts also require strategic preparation of pre-clinical and early clinical data for EVH-supported prototype candidates against pathogens with epidemic or pandemic potential. The pre-clinical and clinical EVH teams will participate in developing master protocols for pre-clinical studies and clinical trials for use during a pandemic. This preparatory work is the cornerstone for accelerated product development in a crisis and is covered in detail below. Ongoing activities, including EVH crisis simulation exercises and audits, will secure the readiness of EVH pre-clinical and clinical services for a pandemic event.

To maintain regulatory readiness, the EVH will support dedicated warm-base regulatory activities, such as scientific advice and the licensure of showcase products. These activities will be documented as case studies illustrating the regulatory pathway and licensure process. Additionally, the EVH will coordinate regulatory preparedness exercises internally and with selected partners. These exercises will include dossier stress tests, mock scientific advice procedures, and scenario-based evaluations of platform technologies. Through these exercises, the EVH will ensure that the procedures, documentation, and regulatory pathways required for pandemic response remain current, functional, and aligned with evolving scientific, regulatory, and legislative developments.

b. Product and Preparedness Support Across the Development Pipeline

The regulatory support framework for product development is structured around the EVH's end-to-end pipeline, ensuring that scientific innovation is consistently aligned with regulatory expectations at every stage. From initial antigen selection and platform qualification through preclinical testing, clinical evaluation, and manufacturing scale-up, the EVH provides targeted, phase-specific guidance to maintain regulatory readiness and accelerate decision-making. This structured approach enables early identification of potential bottlenecks, standardises critical documentation, and ensures that both internal and external candidates can progress efficiently toward emergency authorisation.

The primary developmental challenge outside of a pandemic or epidemic is generating credible efficacy evidence in the absence of a circulating pathogen and, potentially, an unknown correlate of protection. To address this, the EVH will support strategies that infer or generate efficacy signals in humans, aligned with the EMA through structured scientific advice. The objective is to evaluate the acceptability of accelerated late-stage product development for epidemic or pandemic situations.

Proactive Regulatory Alignment & EMA/ETF Engagement

A core component of this strategy is continuous, early engagement with the EMA, its Emergency Task Force (ETF), and national competent authorities. EVH partners will work directly with regulators to clarify expectations for product candidates, platform technologies, analytical methods, clinical trial designs, and manufacturing processes. For some candidates, this includes developing prototype vaccine IMPD files and study protocols up to early clinical phases, to obtain regulatory acceptance on the overall development strategy as early as possible, ideally before a crisis emerges. Such early interactions reduce uncertainty, minimise the risk of mid-development redesigns, and ensure that critical components - such as platform-specific but vaccine-agnostic release specifications, validated quality control methods, and requirements for generation of stability data are defined in advance. Drawing on the EMA's evolving position on platform technologies and prior knowledge, the EVH will also support developers in navigating non-clinical evidence requirements, adaptive trial designs, and rolling submissions. Evidence from recent exchanges with the EMA-ETF demonstrates that emergency authorisation may be feasible based on non-clinical efficacy and bridging data supported by robust immunogenicity and safety profiles, underscoring the critical importance of early alignment on evidence expectations.

To operationalise this approach, the EVH has established phase-specific support measures that guide candidates from discovery through to regulatory submission. These measures are designed to ensure fast, predictable implementation while remaining adaptable to new scientific and regulatory developments. The following subsections detail how regulatory support is integrated into each step of the development pipeline, with continuous refinement based on gained experience and emerging insights.

1. Discovery and Early Development

Prevention and treatment of infectious diseases with epidemic or pandemic potential starts with research and discovery of vaccine and mAb candidates. EVH focuses on the design of antigens, vaccine technology platforms such as mRNA and viral vectors, and discovery of mAbs against emerging viral pathogens.

A strategic priority is embedding regulatory foresight into the earliest stages of candidate development. By aligning antigen selection, platform choice, and target product profiles (TPPs) with regulatory expectations from the onset, the EVH ensures that scientific innovation is systematically integrated into viable development pathways. This strategic alignment encompasses a structured assessment of the platform suitability across multiple dimensions, including immunological mechanisms, anticipated clinical endpoints, safety profiles, manufacturing feasibility, and evolving regulatory standards. Scientific advice will serve as a foundational mechanism to validate platform readiness and TPP feasibility against EMA expectations, establishing a coherent trajectory that minimises mid-development pivots and accelerates progression toward clinical evaluation.

Equally important for later applicability, affordability, and access is the strategic integration of intellectual property and freedom-to-operate assessments into early development planning. By proactively mapping potential IP constraints and identifying mitigation pathways, the EVH will enable its developers to make informed decisions regarding platform

selection and formulation design before substantial resources are committed. Complementing this, the EVH will establish a forward-looking data management and digitalization strategy that aligns early experimental design with downstream regulatory and manufacturing requirements. This ensures that foundational research generates structured, submission-ready evidence packages, reducing redundancy and creating a seamless transition from discovery to clinical and CMC development.

In summary, EVH decisions on use of platform technologies will be guided by the pre-defined criteria listed below. To mitigate risks that could hinder vaccine and mAb development in a crisis, the EVH will prioritize technological and regulatory readiness scores in pandemics. Scoring criteria for inter-pandemic periods will be distinct because the EVH will prioritize innovation potential to secure innovation uptake by contributing to the development and establishment of platforms.

Table 1: Criteria for Selection of Platform Technology

EVH Assessment	Pandemic use	Pre-Pandemic establishment
Technological readiness	+++	++
Regulatory readiness	+++	+
Freedom-to-operate	++	++
Follow-up cost	++	+++
Yield	+++	+++
Innovation	+	+++

2. Preclinical Development

The EVH's preclinical strategy centres on establishing standardised assessment frameworks that align early evidence generation with regulatory expectations. Rather than treating preclinical development as a stand-alone phase, the EVH integrates platform-specific data requirements, alternative testing systems, and toxicology design. This ensures that first-in-human studies are prepared through the availability of essential data packages that satisfy the regulatory requirements without unnecessary duplication or delays.

A core element is the systematic leverage of platform-based knowledge across pathogens. By working directly with the EMA and national competent authorities, the EVH will establish clear criteria for when and how existing non-clinical and bridging data can be reused. This reduces redundant studies and accelerates readiness for emergency authorisation. Regulatory coordination will be structured to prepare and maintain clear approval pathways for in vivo studies, keeping development timelines predictable.

Equally important is the integration of novel preclinical methodologies. The EVH will pursue regulatory qualification of organoid systems, high-throughput immunogenicity assays,

computational modelling, and AI-enabled tools as part of a structured evidence framework. These approaches are positioned as complementary tools that enhance early safety and efficacy assessment, reduce reliance on traditional animal models, and thus align with EMA regulatory science priorities. Through sustained regulatory dialogue, the EVH will work to embed these methods into streamlined preclinical packages, creating a more efficient and robust pathway to first-in-human trials.

3. Clinical Development

The EVH's clinical development strategy centres on a preparedness framework that shortens the time between candidate selection and clinical testing during a crisis. Rather than designing protocols from scratch when an outbreak occurs, the EVH will establish standardised master protocols for Phase I/II trials in advance. These templates incorporate adaptive designs, harmonised immunomonitoring strategies, and clear criteria for dose escalation and cohort expansion. Aligning these protocols with the EMA and the EMA-ETF expectations through formal scientific advice ensures that trials can be activated quickly without compromising scientific or regulatory standards and extensive protocol development during a PHE.

A coordinated European clinical trial network is essential to implement these protocols consistently. The EVH brings together experienced vaccine trial sites that enable a coordinated and fast response in emergency vaccine development through standardization of safety reporting, sample handling, and immunogenicity assays, shared data management systems, and alignment of ethics procedures. This structured approach can be extended to collaborating clinical trial networks within and outside the EU and thereby strengthens Europe's capacity to run high-quality, multinational trials rapidly when a pathogen emerges.

Generating credible efficacy evidence before a pathogen is circulating and correlates of protection are known remains a persistent challenge. The EVH intends to address this by developing and validating alternative evidence strategies, including immunobridging, Controlled Human Infection Model (CHIM) studies where feasible and ethically appropriate, and other innovative approaches. These methods will be integrated into the trial framework to support timely regulatory and public health decisions. Coupled with real-time digitalized data analysis and pre-aligned regulatory pathways, this approach allows rolling reviews to run in parallel with ongoing clinical development. To ensure smooth execution, the Hub will also provide targeted training on regulatory requirements for first-in-human studies, keeping trial teams ready to initiate work without delay.

4. CMC and Manufacturing

The warm-base concepts outlined earlier apply directly to platform-based product development. Product-specific regulatory support will leverage the EVH's associated warm-base infrastructure, knowledge base, and protocols to accelerate individual product development, while providing targeted guidance where development diverges from pre-established paths. A central element of the EVH preparedness model is the establishment and maintenance of a portfolio of platform technologies with prior experience for known pathogens that can be rapidly adapted to emerging threats.

Each platform technology will be supported to establish a technology-specific Chemistry, Manufacturing and Controls (CMC) master file containing standardised manufacturing documentation, qualified analytical methods, validated quality control assays, stability data, and a harmonised data environment. By maintaining platform-specific expertise, manufacturing capabilities, and regulatory documentation, the EVH minimises development work during an outbreak. Platform CMC master files, including core elements of the Investigational Medicinal Product Dossier (IMPD), will contain manufacturing processes for drug substance and drug product, analytical methods, stability protocols, batch release specifications, and quality control strategies. Where appropriate, these established methods and specifications can be adapted to candidates targeting newly emerging pathogens, substantially reducing CMC development effort and regulatory submission timelines. EVH will seek a routine mechanism for alignment with the EMA and ETF on the content, maintenance, and regulatory acceptance of these platform master files, which will initially be pursued through preparatory exchanges and Scientific Advice, ensuring they are endorsed by regulators and ready for rapid reference during an outbreak.

Manufacturing capacity is a critical determinant of Europe's emergency response capability. Building on existing initiatives such as the EU-FAB network and warm-base capacities established through ZEPAI, the EVH will identify and engage agile contract manufacturing organisations (CMOs) with expertise across multiple platform technologies. Facilities will be selected based on GMP readiness, technology transfer capabilities, and the ability to rapidly implement pre-validated manufacturing processes at scale, including production of critical components. Standardised manufacturing templates, validated analytical methods, and harmonised quality control strategies will facilitate rapid transition from clinical to commercial-scale production. To further strengthen manufacturing preparedness, the EVH will cooperate with partners to pre-qualify facilities, secure surge capacity, validate scale-up strategies, and address regulatory requirements for critical raw materials and supply chains. Planning for technology transfer and process validation will ensure manufacturing can commence rapidly and reliably once a candidate is prioritised. Finally, the EVH will support research to strengthen crisis-ready manufacturing and quality systems, including rapid scale-up strategies, harmonised batch release procedures, digital quality infrastructures, and resilient supply chains. Building on lessons from the COVID-19 pandemic, the EVH will collaborate with manufacturers, regulators, and standardisation bodies to generate the evidence needed to support rapid, scalable, and regulatory-compliant manufacturing during future public health emergencies.

c. Measures to Accelerate EVH Developments

The EVH's acceleration strategy moves beyond traditional regulatory alignment by embedding novel methodologies and standardised frameworks directly into the development pipeline. By pre-emptively addressing systemic barriers that might impede the seamless and rapid development of emergency vaccines and mAbs, the EVH aims to establish a stringent procedure for regulatory compliance to increase predictability and efficiency in pandemic countermeasure development and licensure. The intention is to provide upfront clarity on approval requirements, reduce developmental and administrative delays, and support faster initiation of clinical trials, accelerated authorisation, and rapid scale-up of mass manufacturing during emergencies. Rather than treating preparedness as

a reactive exercise, the EVH proactively integrates platform-specific regulatory science, pre-qualified manufacturing protocols, and adaptive clinical frameworks to compress timelines without compromising safety or quality. To achieve this, the EVH is implementing the following targeted methodological interventions:

1. Systematic Leverage of Prior Knowledge & Cross-Pathogen Evidence Generation

A cornerstone of the EVH acceleration strategy is the systematic identification and validation of prior knowledge that can be leveraged across pathogens using the same platform technology. If a platform is already approved for another product, the need for repeated toxicology studies could be reduced or waived. Clinical safety data from earlier platform candidates could also provide valuable context for assessing new candidates. The EVH will establish clear, regulator-aligned criteria for when and how platform-based tox, safety, and CMC data can be reused, ensuring developers avoid redundant studies while maintaining rigorous safety standards. By mapping these knowledge assets early, the Hub will compress development timelines, reduce duplication, and create a predictable regulatory pathway for same-platform products. To operationalise this approach, the EVH will consolidate these validated data packages into structured, platform-specific documentation that regulators can reference consistently.

2. Platform-Specific Master Files & Harmonised Data Infrastructure

This consolidation takes the form of platform-specific master files - standardised regulatory assets that bundle qualified analytical methods, stability data, immunogenicity readouts, and pre-validated tox and safety summaries into a single, reusable framework. By maintaining these documents in a state of operational readiness, the EVH eliminates the need to rebuild foundational documentation during an outbreak. Developers can instead focus on pathogen-specific optimisation. The Hub will also establish platform-specific criteria for quality control strategies and batch release, enabling rapid technology transfer and pre-approved quality frameworks. This harmonised data environment supports prototype vaccines that can progress to Phase II before a crisis, ensuring meaningful, regulator-ready data are available for emergency deployment.

3. Manufacturing Networks & Risk-Adapted Quality Strategies

Accelerating scale-up requires methodological shifts in how manufacturing capacity is structured and validated. The EVH is building on the EU FAB network to pre-qualify agile CMOs/CDMOs across multiple platform technologies, selecting facilities based on GMP readiness, technology transfer capabilities, and adherence to pre-agreed manufacturing protocols. This pre-destined network ensures rapid production of clinical lots and critical components (e.g., LNPs, viral vectors). To further reduce bottlenecks, the EVH is implementing risk-adapted QA/QC concepts and need-based manufacturing strategies. These methodologies allow for streamlined batch release, harmonised quality control, and faster transitions from clinical to commercial scale, ensuring Europe can produce sufficient doses for trials and population deployment within months rather than years.

4. Innovative Regulatory Pathways & Pre-Consented Clinical Frameworks

The EVH is pioneering regulatory methodologies that decouple scientific and regulatory review from sequential timelines. By securing early alignment with the EMA on platform-

specific characteristics, the EVH enables rolling submission pathways where regulatory assessment begins as soon as key data become available. This approach leverages platform consistency to reduce redundant non-clinical requirements and, where predefined criteria are met, allows for smaller clinical datasets supported by robust immunogenicity and safety bridging data. Complementing this, the EVH is developing pre-consented clinical trial templates, including platform trials, Controlled Human Infection Model (CHIM) studies, and validated immunobridging approaches. These frameworks, combined with digitalised data analysis and adaptive trial designs, enable seamless phase progression and parallel regulatory review. Together, these methodologies transform clinical development from a linear process into an agile, data-driven system that accelerates evidence generation while maintaining regulatory compliance.

d. Education and Training

Accelerated vaccine and monoclonal antibody development requires a workforce equipped with up-to-date regulatory, scientific, and manufacturing expertise. The EVH will therefore implement targeted training initiatives to strengthen regulatory literacy and compliance across its partner network. Given that novel candidates will be (co-)developed primarily in academic settings, early training on regulatory requirements, manufacturing, and product development will be essential. This includes anticipation of the upcoming European legislative framework, which - building on the experience gained in the COVID-19 pandemic – shall provide a legal basis for phased review of data packages for licensure.

These educational initiatives will build upon existing DZIF training frameworks while actively mobilising the expertise of EVH members and external stakeholders to develop novel, practice-oriented concepts to increase literacy in this area. By embedding regulatory awareness into the early stages of research and development, the EVH aims to improve adherence to regulatory standards, reduce mid-development redesigns, and accelerate timelines from discovery through clinical evaluation. Training will be delivered through structured workshops, symposia, and hands-on modules tailored to the specific needs of academic developers, industry partners, and regulatory affairs professionals within the EVH.

III. Accelerate European vaccine development and manufacturing

Accelerating European vaccine and monoclonal antibody development for the next PHE requires more than internal readiness of the EVH. It also requires developments on a regional and international level - both in policy and in practice. This demands a proactive understanding of how the regulatory system functions, where it can be streamlined, and how emerging methodologies can be systematically integrated into the European framework. Through targeted regulatory intelligence, cross-sector research, and structured stakeholder interaction, the EVH will evaluate current frameworks, identify operational bottlenecks, and generate evidence-based insights that inform regulatory practice and could shape future policy development. We aim to translate scientific and manufacturing innovations into actionable regulatory knowledge, and to promote a more agile, predictable, and resilient European system capable of responding to future pandemics.

a. Regulatory Intelligence

Regulatory intelligence is the foundation of anticipatory preparedness. It requires the continuous monitoring of evolving principles, the identification of systemic constraints, and the proactive alignment of European frameworks with global best practices.

Monitoring of Regulatory Trends and Technology-Specific Developments

The EVH will serve as a focal point for regulatory intelligence at the forefront of pandemic and crisis-driven vaccine development. By systematically monitoring regulatory and technological developments across the EU and globally, the EVH will remain agile in responding to emerging trends and ensure the seamless integration of innovation into its development pipeline. This intelligence gathering will explicitly track EMA's regulatory science strategy, ICMRA, the Innovative Health Initiative (IHI), CEPI outputs, and WHO guidance on emergency use pathways, translating these insights into practical guidance for EVH partners.

As an example, the ongoing revision of the upcoming EU pharmaceutical legislation introduces key mechanisms to support faster and more predictable development and regulatory assessment, including certified platform technology master files (PTMF), which allow marketing authorisation applications to rely on previously assessed platform data, as well as Temporary Emergency Marketing Authorisations (TEMAs) for medicinal products needed during a recognised PHE. As explained above, the EVH will anticipate these changes and contribute to practical implementation via best practice examples. In addition, the proposed European Biotech Act will streamline and harmonise the regulatory framework for clinical trials, including multinational trials, by simplifying procedures and reducing authorisation timelines. The EVH will anticipate these upcoming changes in the coordination of its development program activities to strengthen regulatory preparedness for pandemic vaccine and monoclonal antibody development in future PHE.

On the technological front, the EVH will actively support the adoption of selected emerging platforms by providing targeted regulatory expertise on development pathways and

marketing authorisation requirements. Within its own operations, the EVH will evaluate and, where appropriate, qualify novel technologies that enable faster development cycles and higher manufacturing yields for vaccines and monoclonal antibodies. For immature technologies that have not yet secured marketing authorisation, this will require the strategic development of prototype vaccines or mAbs. Crucially, these efforts must extend beyond first-in-human trials to systematically build the required knowledge base, generate comprehensive data packages, define technical specifications, and establish the regulatory evidence needed to secure acceptance as a viable option for future pandemic response.

Identification of regulatory challenges and solutions

To further accelerate crisis-driven developments, the EVH intends to actively contribute to European and global harmonisation of regulatory expectations. Reducing fragmentation and establishing multi-country clinical trial protocols and agreement on and adoption of regulatory requirements is essential for reliable and fast development of medicinal countermeasures. The EVH will contribute to solidifying these efforts wherever possible and seek exchange and alignment with stakeholders with common interests in the field. Specifically, the EVH actions will complement ongoing programs arising from EMA's regulatory science strategy, the Coalition for Epidemic Preparedness Innovations (CEPI) outputs, and contribute to the improvement of World Health Organisation (WHO) guidance on emergency use pathways where relevant and participate in EU and international programs to facilitate collaboration. Most importantly, the EVH will deliver best practice examples from within or outside the EVH to ensure that innovation, knowledge, data and methodology are translated into practical implementation that ensures that EVH crisis development plans adhere to the latest regulatory expectations and scientific standards.

b. Regulatory Methodology

Regulatory research within the EVH is structured to identify practical barriers in vaccine and mAb development and translate scientific findings into clear regulatory guidance. Rather than relying on ad hoc consultations, the EVH relies on a systematic approach to map knowledge gaps, evaluate emerging methodologies, and align regulatory expectations with real-world development capabilities. This includes structured stakeholder engagement, evidence-based assessment of platform technologies, and continuous feedback between scientific innovation and regulatory practice. The goal is to streamline approval pathways, reduce duplication, and ensure that European preparedness remains aligned with evolving scientific and legislative developments.

Think Tanks

As a core part of this approach, the EVH will convene regulatory think tanks bringing together experts from private, public, and academic sectors, including small developers, regulatory agencies, key opinion leaders, policymakers, etc. These workshops will focus on cross-cutting issues that delay regulatory approval in multinational clinical trials and licensure, particularly around platform technologies, crisis-ready manufacturing, and clinical development strategies. Discussions will centre on defining the data sets required for

regulatory decision-making, including frameworks for AI and real-world evidence, as well as practical barriers such as cross-jurisdictional data sharing. To ensure impartial and focused dialogue, these exchanges will adhere to Chatham House rules.

These think tanks will complement other EVH activities by mapping the existing data landscape and verifying the subjects where regulatory decision-making is needed. They will further contribute to the outlining of practical steps to shorten development-to-licensure timelines and support systemic regulatory harmonisation across Europe. The insights generated will feed directly into the EVH's ongoing development programs, the Vaccine Readiness Plan and the Stakeholder Network, enabling knowledge transfer and faster adaptation before and during PHE.

Case Studies: Best Practice Examples for Innovation Uptake

Translating technological and regulatory innovation into practice requires practical implementation and verification. To this end, the EVH has developed a case-study approach to test regulatory readiness and assess the feasibility of deploying new technologies or vaccine/mAb prototypes during a pandemic. Two scenarios are outlined below to illustrate how these exercises will generate actionable knowledge on regulatory pathways for candidate vaccines advancing to late-stage clinical development and approval. Potential candidates will be selected through EVH expression-of-interest calls.

Case Study A: Phase 3 Readiness for Rapid Pandemic Response

Objective: ***Evaluate the feasibility of preemptive emergency vaccine development up to Phase 2 to enable rapid generation of efficacy data during an epidemic or pandemic.***

Prototype vaccine candidates against potential epidemic or pandemic pathogens will be advanced from early development through to the end of Phase 2. At this point, clinical safety and immunogenicity data will demonstrate an acceptable safety profile and induction of humoral and/or cellular immune responses. Concurrently, scalable manufacturing processes and quality control concepts will be well advanced, with formulation studies and stability assessments of drug substance and product either completed or ongoing. Building on CMC development and non-clinical/clinical safety and immunogenicity data, an IMPD and a Phase 3 efficacy trial protocol will be prepared. These documents will be reviewed by national competent authorities and the EMA in a Scientific Advice meeting to confirm formal acceptability and align on critical elements.

Clinical trial sites will be pre-selected and coordinated to enable a rapid, multinational Phase 3 launch if an outbreak occurs. EVH will harmonise and align the clinical trial network within its consortium, while establishing collaborations with trial sites in outbreak-prone regions (e.g., Africa, South America, and Asia) to ensure late-stage clinical development can be quickly resumed and collaborative efficacy data generated locally.

Depending on the manufacturing process and involved CDMO/CMO, additional preparatory activities will include scale-up simulations to generate required comparability data, technology transfer protocols, product-specific warm-base concepts, and batch release testing protocols using clinical trial material for a large Phase 3 study. All activities will be

planned and aligned with national authorities and the EMA. Development will then be placed on hold. If an epidemic or pandemic emerges that matches the candidate, the pivotal Phase 3 study will be activated immediately using the pre-established network and approved protocol.

Case Study B: Pre-Pandemic (conditional) Marketing Authorisation
Objective: ***Evaluate the pathway to conditional marketing authorisation for a vaccine candidate intended for epidemic or pandemic use.***

Where scientifically and regulatorily justified, a pandemic vaccine candidate will be developed to the point of a European Conditional Marketing Authorisation or a Marketing Authorisation under exceptional circumstances. This requires non-clinical efficacy data in a suitable animal model, combined with human immunogenicity and safety data that meet regulatory standards for conditional approval even in the absence of an active outbreak. Initial specifications and regulatory expectations will be discussed early with the EMA and national competent authorities. The EVH will also engage with regulators to define requirements for product launch, including manufacturing and deployment, as a prerequisite for pandemic readiness.

The proposed development pathway includes the following steps:

I. Clinical Development

Clinical Safety Database: A safety database comprising approximately 3,000 participants will be generated to support the marketing authorisation application.

Inferring Clinical Efficacy: Several vaccines against emerging pathogens have received conditional marketing authorisation in the EU without direct clinical efficacy data. The EVH will evaluate the following approaches to infer efficacy:

• Passive transfer studies using serum or purified monoclonal antibodies from vaccinated subjects in susceptible animal models to assess protective capacity. If efficacy relies solely on animal data, post-approval observational effectiveness studies in humans will likely be required.

• Immunobridging studies focusing on immunogenicity data to predict clinical protection when a licensed vaccine for the same pathogen exists and a correlate of protection is established. This approach is suitable for vaccines relying on pathogen-directed humoral immunity, as efficacy can be assessed using laboratory assays.

• Controlled Human Infection Models (CHIMs), or human challenge studies, which expose selected healthy volunteers to a well-characterised pathogen under controlled conditions after vaccination. CHIMs require an available rescue therapy and typically need fewer participants than field trials, as infection is assumed. When ethically appropriate, they can enable rapid efficacy assessment and allow parallel testing of multiple candidates, formulations, or dosing regimens to inform subsequent larger trials.

II. Manufacturing and Marketing Authorisation Holder

Advancing a vaccine candidate to conditional marketing authorisation will likely require collaboration with an EU-based pharmaceutical industry partner acting as the Marketing Authorisation Holder (MAH). The MAH would be responsible for epidemiology-driven

updates to the vaccine (e.g., optimising targeting of emerging variants), pharmacovigilance monitoring, risk-management and manufacturing process adjustments (e.g., scale-up), as well as submitting the marketing authorisation application in the EU and beyond. This industry-led model enables rapid vaccine availability during an outbreak by supporting pre-pandemic manufacturing and warm-basing. To expand capacity for pandemic preparedness, additional manufacturers (CMOs) or sites would need to be qualified through technology transfer led by the MAH. However, unpredictable epidemiology and uncertain return on investment pose significant risks to this approach. The EVH will therefore also explore alternative models and the conditions required to ensure their long-term sustainability.

c. Regulatory Research Concept

The regulatory research concept defines how EVH will contribute to the advancement of regulatory science in areas directly relevant to pandemic preparedness. Its purpose is to generate evidence, methodologies and tools that support regulatory decision-making, applicable in accelerated development, guidance documents, pharmaceutical legislation and licensure of vaccines and monoclonal antibodies. This research agenda is grounded in the needs identified in the think tanks organised by the EVH or through interactions with EMA, vaccine industry, national competent authorities, IHI projects and international EVH partners. Its purpose is to address the regulatory bottlenecks that impede rapid response during health emergencies.

EVH will establish the basis for a coordinated research program that focuses on platform technologies, innovative clinical trial designs and immunoassays, new approach methodologies (NAMs), implementation of digitalisation and AI as well as crisis-ready manufacturing systems. The aim is to accelerate vaccine development and address knowledge gaps, to enable regulatory decision-making by provision of meaningful data thus reducing uncertainty and risks associated with product development in pandemics. Notably, these areas reflect the priorities highlighted in EMA's regulatory science strategy and the EU Pharmaceutical Legislation, which emphasise the need for evidence-based approaches to accelerate development and regulatory decision-making. A key focus will be the generation of evidence to support **platform-based development strategies and the shaping of regulatory pathways** as a mainstay of preparedness. This includes defining the data required to demonstrate platform consistency, analytical comparability and cross-pathogen applicability. EVH will work with partners to develop standardised CMC packages, qualified analytical assays and harmonised data structures that can be reused across multiple pathogens. This work will build on EMA's evolving position on prior knowledge and platform technologies, as presented in the EMA webinars and legislative proposals. Importantly, the EVH will seek to develop practical validation and implementation concepts to extend the platform concept beyond manufacturing and formulation to clinical efficacy and safety.

EVH will also advance **innovative clinical trial methodologies**, including human challenge trials using Controlled Human Infection Models (CHIM), adaptive designs and platform trials, decentralised approaches, and explore the conditions that allow the integration of real-world evidence or early transition into phase 4 post-marketing trials. Strategic combination of these

approaches is essential for accelerating clinical development and enabling regulatory review to begin as soon as relevant data are available. EVH will support the development of harmonised templates, statistical frameworks and operational models that can be adopted across member states, reducing fragmentation and enabling more efficient multi-country trials.

In the area of new approach methodologies, EVH will promote the development, validation and method qualification of in vitro, in silico and ex vivo systems that could reduce reliance on animal models and accelerate early development or predict vaccine efficacy when used for evaluation of early clinical trial samples. This aligns with EMA's emphasis on NAMs as a key regulatory science priority and supports the broader EU objective of reducing animal testing where scientifically justified.

Finally, EVH will support research on **regulatory aspects of crisis-ready manufacturing and innovative patient-centred approaches to quality control**, including rapid scale-up simulations, manufacturing technology for increased yields to advance suitability for mass manufacturing of viral vectors, consistency- and risk-based QC and batch release strategies and digital quality infrastructures. This work will draw on lessons from COVID-19, where supply chain bottlenecks and fragmented quality systems slowed down vaccine deployment although marketing authorisations and mass manufacturing were in place. EVH will collaborate with manufacturers, competent authorities and standardisation institutions to collect data for the generation of evidence-based approaches for rapid, scalable and compliant production and testing in emergencies.

IV. Partnership and Communication

Accelerated product development and regulatory processes require trans-disciplinary exchange, communication and education. The EVH is aware of the importance of these topics and will implement communication streams to foster transparency, information and exchange. The last pandemic exposed widespread public mistrust in vaccine development and regulation, which was exacerbated by the accelerated processes. In a pandemic-resilient society, vaccines must not only be safe and effective, but they should also be perceived as protective measures by the public. The EVH embraces its responsibility to strengthen public trust within the project's scope. We will therefore communicate EVH activities and regulatory developments transparently by reaching out to experts, researchers, and the public. In this line, the EVH will collaborate with initiatives addressing vaccine hesitancy and will seek dialogue with vaccine developers, patients, and other stakeholders to build stronger trust in vaccine development, regulation, and deployment.

Regulatory research and practice remain a transdisciplinary cross-sectional topic requiring input from diverse stakeholders across academia, public health, private industry, and government. It is therefore imperative to connect across these domains to enable novel approaches in regulatory sciences. Within Europe, regulatory research remains fragmented with limited opportunities for transdisciplinary exchange. This gap has recently been partially addressed through the establishment of the European Platform for Regulatory Science Research in 2025 by the EMA, to which the EVH's regulatory work package will also

contribute. However, as the platform is hosted by the EMA, it can only address topics of common interest within the existing framework.

Given the unmet need for an impartial exchange on regulatory topics specifically in preparation for public health emergencies, the EVH will establish topic-specific transdisciplinary networks to address emerging challenges. Most exchanges will be organised as Think Tanks, symposiums or workshops. These events will contribute to the EVH's larger Stakeholder Network, a foundational element of the cross-sectional identity of the EVH. Building a robust network will enable reliable and durable information exchange and facilitate developments that strengthen European regulatory preparedness for future pandemics. During a pandemic, an established network can also adapt more swiftly to unprecedented challenges. Participants and associated institutions will further enhance their expertise and awareness of regulatory decision-making in public health emergencies.

V. Concluding Remarks and Outlook

Pandemic preparedness is an evolving field, highly dependent on technological progress, changing legislative and regulatory frameworks, and societal perceptions. The EVH scope is to foster innovation and to streamline the translation of product candidates from the discovery and preclinical stages into reliable and efficient clinical product development to ensure early access to vaccines and mAbs to combat pathogens during a pandemic. The EVH regulatory strategy outlined in this document is therefore designed to adapt innovation and to support European pandemic preparedness through an agile, anticipatory approach. This underscores that continuous improvement - and, where necessary, strategic transformation - must serve as the driving force and foundation for long-term pandemic resilience.

Marburg, 31.8.2026

Author: Isabelle Bekeredjian-Ding*(bekeredjian-ding@uni-marburg.de), Nadine Kirsch-Stefan, Rita Fröde, David Mentrup, Shashank Pinnapireddy, Klaus Cichutek, Poleta Luga, Svein Ruine Anderson on behalf of the EVH Consortium

DOI: https://doi.org/10.17192/openumr/1116

Contact: evh@uni-marburg.de

Co-funded by the European Union

Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or HERA or EMA. Neither the European Union nor the granting authority can be held responsible for them.