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CIRM Access and Affordability Planning Requirements

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Access and Affordability at CIRM

CIRM is committed to ensuring that every BLA-ready regenerative medicine program has a strategy for access and affordability. Applicants to Preclinical (PDEV) and Clinical (CLIN2) funding opportunities are required to provide stage-appropriate plans for access and affordability that will be evaluated during scientific review and maintained as awards progress. Complementary activities to support commercialization and market access are also recommended to advance these therapies to patients. This guidance document is intended to help applicants understand and implement access and affordability planning, and to serve as a resource for recommended commercialization and market access activities.

Resources

CIRM has collaborated with external consultants and the Access and Affordability Working Group (AAWG) to identify activities supporting access and affordability, activities supporting commercialization and market access, and to develop a rubric to evaluate adequacy and appropriateness of access and affordability activities. These resources are included as appendices to this document.

Appendix A: Access and affordability planning requirements by program stage

Appendix B: Description of access and affordability activities

Appendix C: Access and affordability activity evaluation rubric (CLIN2 program only)

Appendix D: Recommended stage-specific Commercialization and Market Access Activities, including instructions on where in the Proposal Template PDEV and CLIN2 applicants should describe plans or completed activities.

Key Terms

Access: the ability of individuals to obtain and use healthcare services, information and resources

Affordability: an individual's ability to afford treatment, testing and other healthcare costs

Commercialization: the process of bringing a product to market, encompassing everything from R&D to manufacturing, marketing and distribution

Market Access: ensuring the right patients receive the right treatments at the right time by effectively navigating healthcare payers, reimbursement policies, and pricing strategies

Preclinical (PDEV) Program Requirements and Evaluation Overview

Application Stage Requirements:

When preparing a PDEV full application, Principal Investigators are required to discuss plans to demonstrate stage-appropriate progress on the following activities during the PDEV award. Applicants should also describe progress and outcomes of completed or in-progress activities, if applicable:

Access and Affordability activities:

- Market landscape assessment/market research
- Reimbursement and market access strategy

Commercialization and Market Access activities:

- IP strategy
- Regulatory pathway strategy
- Financial planning and fundraising strategy
- Technology transfer and scalability planning
- Partnerships and collaborations

Application Stage Evaluation:

Access and Affordability activities will be evaluated by the Grants Working Group (GWG) as part of the Value Proposition and Project Plan & Design review criteria. Please review the PDEV Program Announcement for a description of these review criteria.

Award Milestones:

Access and affordability plans will be incorporated into PDEV award Operational Milestones as described in the PDEV Program Announcement. PDEV awardees will be required to report progress on commercialization and market access activities over the course of the PDEV award.

Clinical (CLIN2) Program Requirements and Evaluation Overview

Application Stage:

Access, Affordability, Commercialization, and Market Access planning are incorporated into the CLIN2 application in two formats:

1. Applicants **are required to complete** an Access and Affordability Planning Proposal, which is available as a template in the Online Application in CIRM's Grants Management System. Applicants must consult Appendix A in this guidance document to identify the prerequisite ("Must have at Entry") and award-stage ("Award Milestone") activities required for each trial stage, and to follow further instructions in the template.
2. Applicants have the option to discuss progress towards completing recommended stage-specific commercialization and market access activities (Appendix D) in the "Clinical Development and Commercialization Plan" section of the Scientific Proposal.

Application Stage Evaluation:

Information provided by CLIN2 applicants in the Scientific Proposal and Access and Affordability Proposal will be evaluated as follows:

1. During Eligibility and Completeness Review, CIRM staff will assess the Access and Affordability Proposal to determine whether applicants have provided descriptions of required prerequisite and award-stage activities based on the trial stage of the project. **Stage-appropriate Access and Affordability activity descriptions are REQUIRED for applications to be considered complete and proceed to review.**
2. External consultants who are subject matter experts in access and affordability will evaluate complete Access and Affordability Proposals according to the rubric in Appendix C. Rubric scores will inform programmatic funding recommendations, applicant feedback, and award management.

Award Milestones:

Access and affordability plans will be incorporated into Operational Milestones as described in the CLIN2 Program Announcement. CIRM may consult with external subject matter experts to assess progress towards completion of Milestones.

Budget Justification Guidelines

Applicants should consider and justify any resources needed to complete proposed access, affordability, commercialization, and market access planning activities. Costs required for these activities must be requested and justified in the submitted application as part of the overall Budget Justification for the project and incurred during the funded project period. Consistent with CIRM's Grants Administration Policy for Clinical Stage Projects, budget requests must not include infrastructure costs that are included in institutional overhead (e.g., awardee's facilities & indirect costs) or costs associated with the routine conduct of research. Costs may not be double charged, or inconsistently charged, as both direct and indirect costs. Resources to cover total cost of access, affordability, commercialization, and market access activities do not solely have to be funded by CIRM.

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Appendix A: Access and Affordability Requirements by Stage

Required Access and Affordability activity name	PDEV		CLIN2 Phase 1 or First in Human		CLIN2 Phase 2		CLIN2 Phase 3	
	Must Have at Entry	**Award Milestone**	**Must Have at Entry**	**Award Milestone**	**Must Have at Entry**	**Award Milestone**	**Must Have at Entry**	**Award Milestone**
Market landscape assessment/market research		✓	✓		✓		✓	
Reimbursement and market access strategy*		✓		✓	✓		✓	
Early revenue and market forecast				✓	✓		✓	
Brand strategy and positioning						✓	✓	
Market segmentation*						✓	✓	
Establish (clinical and payer) advisory board						✓	✓	
Value message						✓	✓	
Quantitative pricing studies*						✓	✓	
Value communication dossiers						✓	✓	
Establish patient registry/Risk-evaluation strategy (post launch)*						✓	✓	
Patient journey*								✓
Pre-approval information exchange (PIE)								✓

Requirements per stage: A table outlining the different Access and Affordability activities expected to be complete at application ("Must have at Entry") and award milestone phases for PDEV and CLIN2 trial stages. For activities designated as required for award milestone phases, applicants must propose plan to

complete those activities during the award period. A * denotes activities with a strong impact supporting access and affordability.

Appendix B: Access and Affordability Activity Descriptions

Activity	Benefits	Strategy
Market landscape assessment/ market research: Conducting detailed market research to assess the potential demand, competition, pricing strategies, and market gaps.	Understanding the size of the market, potential customers, unmet needs, and potential barriers to entry.	Perform in-house research reaching out to providers/payers/advocacy groups, and other key stakeholders. Utilize free online industry reports to inform market assessment. Consider minimal investment options for acquiring therapeutic area/industry market reports.
Reimbursement and market access strategy: Planning for the product's reimbursement strategy by assessing the healthcare landscape, payer preferences, and pricing models.	Early understanding of the product's economic value to health systems and key stakeholders is important for successful adoption in the market. During clinical stages outline an evidence generation plan for a product to ensure the "right" data will be available for regulators and reimbursement authorities to justify value and pricing.	Ensure market research is executed highlighting where the product fits into the clinical paradigm. Conduct early pricing studies to understand the price corridor that might be acceptable from the perspective of payers and providers given the attributes of the Target Product Profile (TPP). Early engagement with payers to understand access hurdles (e.g., prior authorizations); understand impacts the new product might have on provider practice in order to facilitate adoption. Continue monitoring and refinement of strategy as the product goes through the development process.
Early revenue and market forecast: Develop early market and revenue forecasts using published evidence and qualitative primary research to understand the target population, peak market share, pricing and resulting revenues.	These analyses are refined throughout the development process and useful for negotiating potential licensing agreements.	Document key assumptions for early forecasts that are developed in house - these assumptions can be validated or refined during subsequent market research. Refine forecasts during the clinical development cycle by conducting robust secondary and primary market research using the TPP, understand where the product fits into the clinical paradigm, and gain insights from IDIs regarding how the product will be perceived, potential market share and price range. Work with a market access/strategy consulting firm with expertise in developing forecasts.

Brand strategy and positioning: Starting the process of brand development, including naming and positioning the drug in the marketplace. Understand how a product is differentiated in the market.	Lay the foundation for future value message development and what drivers of value are important to physicians, patients, payers and other stakeholders. Attract funding to support future development.	Ensure market research is executed highlighting where the product fits into the clinical paradigm; research with payers and providers will give insight into how the product will be perceived. Early in the development process, establish a clear vision for the product outlining the unmet need and how the product will meet the need. Later in the development process, develop a brand strategy that identifies the target patients/providers, define the brand by what messages are to be communicated, and lastly develop a positioning statement. This activity will require the value message development to be completed.
Market segmentation: Segregate potential customers (e.g., patients/providers/payers) into groups based on different characteristics (e.g., geography, demographics, behaviors, etc.).	Key benefits include the ability to optimize marketing effort, enhance adoption and brand competitiveness.	Identify datasets that allow for identification of site of service and healthcare provider (HCP) prescribing behaviors.
Establish (clinical and payer) advisory board: Identify key opinion leaders who could serve as advisers. Periodically seek feedback on clinical and economic evidence generation efforts. Periodically develop content for advisors to review and provide feedback to support the development process.	Clinical and payer key opinion leaders (KOLs) offer expert advice as the development program progresses through the clinical stages of development through commercial launch.	Develop logistics to follow relevant company and local rules and laws when organizing an advisory board meeting. Consider outsourcing the organization, logistics, agenda, content development and meeting out-put analysis/reporting to a contractor to assist unless in-house company support is available
Value message: Develop value messages that communicate key drivers of value, which is supported by evidence that helps differentiate a therapeutic in the marketplace.	Value messages help clearly communicate the benefits of a drug to various stakeholders, including regulators, payors, healthcare providers, and patients. This ensures that everyone understands the therapeutic and economic value of the drug.	Conduct early market research (i.e. pre-clinical or Phase 1) into the market landscape, unmet needs, and disease burden. Developing the TPP and evidence generation plan, early economic modeling will all contribute to charting the path to developing the right data required to support justifying the value and pricing of a product. Refine message as the product moves through the development stages. Conducting advisory board meetings are useful for testing what data and messages resonate most with key stakeholders in

		terms of communicating the value of a product.
Quantitative pricing studies: Conduct a robust conjoint analysis to understand the impact of product attributes have on price from the perspective of payers and other key stakeholders.	Understand the market acceptable price given demonstrated product attributes. Ability to optimize price and market share to maximize revenues.	In rare/ultrarare disease areas leverage other research studies (e.g. cost-effectiveness analysis, budget impact model, advisory boards, qualitative pricing research) to inform pricing decisions. In other cases, wait for the development program to reach Phase 3 and initial pivotal data becomes available. At this point the investment risk is minimized by the product reaching the end-stage of development. Work with a vendor with access to large numbers of HCPs and payers for recruitment, and with expertise of programming surveys for simple data collection. Build in safeguards such as screening questions as part of the survey design to minimize risk of unreliable data.
Value communication dossiers: Development of the Academy of Managed Care Pharmacy (ACMP) dossier for the US (pre-approval/final approved versions) and Health Technology Assessment (HTA) submission dossiers for Ex-US markets	As part of the technology assessment, US payers typically request an AMCP dossier for new interventions. Other HTA bodies have a different dossier format to communicate similar content, although it is usually more detailed.	Ensure available evidence is collected (e.g. market research, systemic literature review, indirect treatment comparison, model reports, clinical study report, pre-launch label, value messages). At minimum, have a draft/pre-launch version developed that can be quickly updated once the price is official (frequently this happens at launch).
Establish patient registry/Risk-evaluation strategy (post launch): Develop a registry for patients to collect long-term, real-world data on the safety, efficacy, and outcomes of the cell or gene therapy or best supportive care or usual care. This activity is required for eligible cell and gene therapy candidates and encouraged for all eligible regenerative medicine candidates.	Enables monitoring of patients treated (or not treated) with the cell or gene therapy over the long-term. Enables quantification and validation of long-term treatment effects including duration of effect and other unknowns at the time of launch. Regulatory authorities, such as the FDA and EMA, often mandate the use of patient registries to monitor post-authorization safety and efficacy of cell and gene therapy drugs. Results may affect reimbursement decisions post-launch.	Develop a study plan, protocol and project plan that outline the scope, purpose/objectives, timeline, patient populations, interventions, outcomes. Assign responsibilities, personnel (incl advisory board), facilities, resource commitment, and contractors to execute and monitor the registry over time. Extract value from the registry from analysis of outcomes and publishing results.

	Can be used to continuously further the evidence base of the disease area by publishing observed outcomes.	
Patient journey: Develop a detailed pathway documenting the patient experience and healthcare service delivery from the point of a patient symptom on-set through diagnosis, treatment and management.	Developing a patient journey helps identifying pain points (unmet needs) and areas for improvement that a new treatment might alleviate and potentially lead to a more seamless and positive patient/provider/payer experience.	Engage with experts with experience in integrating data from diverse sources to streamline the process.
Pre-approval information exchange (PIE): Develop a presentation to proactively share and educate Payers in the US about certain health care economic and scientific information about new emerging products.	Market readiness tool that is used to facilitate early market access conversations with payers before FDA approval. Helps prepare the market for anticipated place in therapy, pricing, clinical trial results, potential indication, and anticipated timeline for FDA approval.	Ensure there is evidentiary support for the Healthcare Economic Information (HCEI) to comply with FDA regulations. Internal training/education on benefits and socialization of best practices on sharing pre-approval HECI as a way to overcome sensitivities to keeping information confidential until launch.

Appendix C: Access and Affordability Evaluation Rubric (CLIN2 only)

External consultants with expertise in access and affordability will use the rubric below to assess progress on stage-appropriate activities in CLIN2 applications. This rubric is specific to the 12 activities that are most relevant to access and affordability outcomes (Appendix B). These activities are assessed during application review and can inform funding decisions and award management. Composite scores and qualitative assessments will be provided as feedback to applicants. This process supports alignment with CIRM's broader policy objectives while ensuring proportional expectations based on stage of development.

Scoring

Each activity is scored using two factors:

1. A Priority Factor based on its relevance to the development stage
    - Not needed for stage: 0
    - Low (Nice to have): 1
    - Medium (Should have): 2
    - High (Must have): 3
2. A Raw Score reflecting applicant progress (from "Not started" to "Completed in last 12 months")
    - Not started: 0
    - Reasonably planned: 1

- In process/partially completed: 2
- Completed but insufficient: 3
- Completed but needs updating: 4
- Completed in last 12 months: 5

Finally, a Composite Score is calculated and used in review discussions and award monitoring. The composite score is calculated as follows:

1. A Weighted Score is calculated as the "(Priority Factor x Raw Score) / 5"
2. All weighted scores are summed across 12 access and affordability activities to yield the total composite score

Appendix D: Recommended Stage-specific Commercialization and Market Access Activities

Unless required as part of the online application or in instructions in the proposal template, these activities are recommended to support commercialization and market access of the proposed therapy. Unless otherwise directed, activity descriptions may be included in the "Commercialization Plan" (PDEV) and "Clinical Development and Commercialization Plan" (CLIN2) sections of the Scientific Proposal Template.

Activity	Description	Stage Recommendation
Intellectual Property (IP) Strategy	Develop a robust IP strategy by securing patents or other forms of IP protection for the compound or technology	**PDEV:** Recommended award activity **CLIN2 FIH/Phase 1, Phase 2, Phase 3**: Recommended at application
Financial Planning and Fundraising Strategy	Estimate the anticipated required funds for the full development process and initiate steps to prepare to secure funding.	**PDEV:** Recommended award activity **CLIN2 FIH/Phase 1, Phase 2, Phase 3:** Recommended at application
Regulatory Pathway Strategy	Understand the options available by indication for regulatory approval. Are there special designations potentially available (i.e. fast track, orphan designation, breakthrough, and priority review) or 505(b)(2) approach? This activity may include consideration for ex-US markets.	**PDEV:** Recommended award activity **CLIN2 FIH/Phase 1, Phase 2, Phase 3:** Recommended at application
Technology Transfer and Scalability Planning	Ensure that IP is protected as patents. Develop plans for processes (e.g. manufacturing, QC) used during pre-clinical studies that are scalable for later clinical trials and eventual commercialization.	**PDEV:** Recommended award activity **CLIN2 FIH/Phase 1, Phase 2, Phase 3:** Recommended at application
Partnerships and Collaborations	Identifying potential strategic partnerships, collaborations, or licensing deals with larger pharmaceutical companies, biotech firms, or research institutions. These partnerships may provide funding, technology, or expertise needed to advance the development program	**PDEV:** Recommended award activity **CLIN2 FIH/Phase 1:** Recommended award activity **CLIN2 Phase 2, Phase 3:** Recommended at application

Establish Natural History of Disease	Track key outcomes that illustrate the natural course of the disease for the current standard of care paradigm.	**PDEV:** N/A **CLIN2 FIH/Phase 1:** Recommended award activity **CLIN2 Phase 2, Phase 3:** Required at entry
Cost of Illness and Standard of Care	Design and conduct studies using real-world data (RWD) to generate real-world evidence (RWE) evidence that supports product value	**PDEV:** N/A **CLIN2 FIH/Phase 1:** Recommended award activity **CLIN2 Phase 2, Phase 3:** Recommended at application
Quality of Life (QoL) Assessment	Include Health-related QoL measures and utility weights in the pivotal clinical trial. May need to supplement with time tradeoff studies if clinical study sample size is not sufficiently large to assess QoL in the relevant health states.	**PDEV:** N/A **CLIN2 FIH/Phase 1, Phase 2:** Recommended award activity **CLIN2 Phase 3:** Recommended at application
Early Economic Modeling	Develop an early cost-effectiveness model based on existing published literature and the Target Product Profile.	**PDEV:** N/A **CLIN2 FIH/Phase 1, Phase 2:** Recommended award activity **CLIN2 Phase 3:** Recommended at application
Briefing Book	Obtaining early scientific advice from health technology assessment bodies on potential data gaps, trial design, and insights on approaches to demonstrating cost-effectiveness.	**PDEV:** N/A **CLIN2 FIH/Phase 1, Phase 2:** Recommended award activity **CLIN2 Phase 3:** Recommended at application