



Policy on Bioethics



Pacira BioSciences, Inc. (“Pacira” or the “Company”) is committed to conducting its clinical trials in accordance with high bioethical standards and clinical guidelines.

Bioethics is defined as ethics applied to medicine and life sciences, primarily concerned with how advances in biology, medicine, and technology affect patient health, human life, and well-being. Our Research and Development (R&D) practices are guided by our commitment to meet the growing expectations of patients and the health care community. As a patient-centered company, Pacira is committed to uphold the highest bioethical standards.

Ethical challenges emerge because of advances in biology and medicine and changes in politics, law, and culture. Our R&D practices are regularly updated to account for scientific and medical innovation and the necessity to comply with all applicable regulatory requirements.

Pacira has established multiple policies and standard operating procedures (SOPs), under the guidance and oversight of our Chief Medical Officer and Chief Legal and Compliance Officer, to ensure a high level of ethics in scientific and medical activities, better stakeholder engagement and greater transparency.

Our mission at Pacira is to provide an opioid alternative to as many patients as possible and address medical needs along the neural pain pathway. This policy provides an overview of our bioethical policies and procedures that ensure the safety of our patients and the integrity of our R&D activities.

Research Integrity and Patient Safety

At Pacira, we believe integrity in R&D, from early-stage research to late-stage development, is vital to ensure the safety of study participants and to the benefit of our clinical trials. Integrity is defined as soundness of moral character and adherence to moral and ethical principles, including honesty, completeness, and truthfulness. Having integrity means doing things the right way—at Pacira, this means never putting a patient in harm’s way.

Pacira is committed to making the safety and well-being of study participants and patients its top priority and to adhere to high scientific and ethical standards regarding the conduct of any clinical trials and the rigor of our manufacturing processes.

Our R&D activities, including all clinical trials, are designed to ensure that all participants enrolled have given their free and informed consent (or assent if applicable) to participate in a trial, either directly or via their legally authorized representative. Study participants and/or their legal representatives must understand the purpose of any R&D activity so that they are able to make an informed decision about whether to participate. Regardless of the objective, all R&D activities are designed primarily to protect the safety and well-being of participants and to guarantee that they or their legal representatives give their voluntary consent/assent based on straightforward and comprehensive information that is expressed in easily understandable, non-technical language, especially for participants who are considered to be vulnerable for any reason.

We believe that the informed consent/assent process is the foundation of ethical recruitment of R&D participants and that informed consent/assent must be granted before any procedure is performed or before any data is assessed. Study participants should always be the focus of this process. Our protocols include evaluating overall health, literacy, mental capacity, age and other circumstances that may potentially make a study participant vulnerable.

We are committed to informing all study participants the information required to assure free and informed consent/assent which includes, but is not limited to:

- The intent and procedures of the study
- Alternative procedures, treatments, or other alternatives to participation in the activity
- Compensation for expenses for participation in the activity
- The distinction between participation in a study and therapeutic care
- Any constraints added to the activity in addition to standard care protocol
- Any potential risks or benefits related to participation in the activity
- Procedures in the case of an adverse event
- Activity interruption or withdrawal of consent/assent
- Access to information before, during, and after the activity

Ethics in Clinical Trials

All R&D activities at Pacira, including all clinical trials, are conducted in compliance with the Principles of Good Clinical Practice (GCP) and international ethical standards—in particular the Helsinki Declaration on ethical principles regarding human experimentation.

As we work towards developing new therapeutic solutions, we dynamically assess our practices and processes within an ethical framework. Maintaining high ethical standards across our R&D activities requires addressing potential challenges that may arise in response to:

- Cultural, political, and economic trends
- Advances in Biology
- Advances in complementary scientific fields
- Priorities in public health
- Requirements for development
- Respect for increased transparency and privacy protection

Pacira is committed to adjusting its R&D protocols to accommodate developments in each of these areas.

Quality Assurance in Clinical Trials

Maintaining integrity and high bioethical standards throughout any R&D activity is a dynamic process that requires continuous oversight and monitoring. This is supported by our overall Quality Policy and other internal policies and procedures. Our Quality Assurance (QA) protocol mandates scheduled operational checks at each clinical trial site to make sure that our R&D data are generated, collected, managed, analyzed, and reported in line with our requirements. The frequency and specifics of these operational checks are determined for all investigative sites by our Clinical Operations department prior to the commencement of the R&D activity. Each investigating site is monitored by a Pacira-designated representative in accordance with each individual R&D activity plan.

Our QA department is responsible for ensuring procedural and objective analysis of all R&D related activities and documents. These responsibilities may include audits of clinical trial sites or external partners.

Risk Management in Clinical Trials

Pacira develops a Study Risk Management Plan to identify and evaluate potential challenges and risks associated with the conduct of a study. The plan includes risk mitigation strategies and allows the study team to be prepared to handle issues if and when they occur. Pacira implements additional study plans to support continual study oversight (e.g., Safety and Medical Management Plans, Protocol Deviation Plans, Clinical Monitoring Plans, Blinding Plans, Data Quality Review Plans, etc.).

In addition, to limit the risk of potential oversights or infractions by a clinical researcher, we have implemented a system of surveillance and onsite clinical trial monitoring that enables early detection of any signals that indicate potential aberrations, enabling us to investigate and, when necessary, implement corrective measures. Our surveillance framework is designed to identify, evaluate, prioritize, and mitigate potential risks caused by potential misconduct. In the event of a serious deviation (e.g., data fabrication, scientific misconduct, or serious non-compliance at investigator sites), we determine the best course of action according to the severity of the situation. Measures may include an in-depth investigation by a cross-functional panel or termination of the trial for that particular investigative site, and notification to the applicable ethics committees and/or health authorities.

Clinical Trial Audits

Pacira conducts audits of company-sponsored clinical trials and select clinical trial sites in order to ensure compliance with the clinical trial protocols and our quality standards. Pacira has established numerous SOPs detailing a framework for good clinical practice audit procedures, under the oversight of QA Management, our QA Auditors or their designees, and Clinical Operations.

Audits of Pacira-sponsored clinical trials begin with a proposed annual audit schedule from our QA Auditors, which is updated annually (quarterly if changes are needed to the annual plan) and is based on information obtained from Clinical Operations. The frequency and overall number of planned audits per calendar year are determined by QA Management and Clinical Operations. Criteria for determining the frequency and number of audits for any Pacira-sponsored clinical trial may include:

- Phase designation
- Results of prior audits
- Complexity of clinical trial design and duration
- Number of patients planned for enrollment
- Number of clinical trial sites

In addition, we reserve the right to conduct an audit ‘for-cause’ in the event of a serious breach and/or suspected fraud or misconduct.

QA Auditors prepare individual audit plans by outlining the scope, criteria, key audit contacts, audit activities, documentation and record requirements and other relevant information necessary to conduct the audit. Clinical Operations provide QA Auditors with all relative documentation relating to the appropriate Clinical Trial as well as site-specific information for review prior to the audit. All audit plans are approved by Clinical Operations and provided to the appropriate audit

site prior to the audit dates.

All audits are conducted according to their approved audit plan. QA auditors conduct a Closing Meeting with audit participants to request clarifications or responses to observations and to summarize their findings prior to the generation of an Audit Report, which documents the information outlined in the audit plan. Audit reports are reviewed by QA Management and approved within 30 days of the Closing Meeting. Audit certificates are then filed in a Trial Master File to document the audit activity.

QA Auditors coordinate with Clinical Operations to request audit responses or any Corrective and Preventive Actions (CAPAs) from audit participants. QA Auditors are responsible for tracking any CAPAs resulting from the audit to completion and conducting periodic follow-up communications with the auditee until all CAPAs have been implemented. As necessary, Clinical Operations will verify implementation and effectiveness of CAPAs on behalf of the auditor.

Ethical Use of Human Biosamples and Stem Cells

R&D activities utilizing human biological samples (HBS) or human stem cells are conducted to improve human health and quality of life. Such samples are important for studies which aim to better understand the intricacies of medical conditions and develop new treatments. On occasion, Pacira will engage with external partners to provide human biological samples for our medical research and training efforts. Any external partners who provide HBS to Pacira are reviewed as part of our vendor audit process and must demonstrate that any delivery, collection, storage, or external handling of HBS are consistent with high ethical standards, including processes which protect the dignity and identity of human donors.

Pacira does not directly collect, store, or handle HBS, nor do we currently utilize human stem cells as part of our medical and biological research efforts.

Ethical Treatment of Animals

Animal research raises ethical issues not only for clinical researchers that use animals as part of their studies, but also for society. Pacira believes that the use of animals in research is justified only when there are evident benefits to human and animal health. As a key element of our bioethical framework, we are committed to meeting all applicable regulations and standards for the use of animals in our studies and to develop alternative approaches to their use whenever possible.

Any study of animals for medical research purposes on behalf of Pacira is conducted by external partners that conform to the high animal use standards set forth by the U.S. Department of Agriculture (USDA) and the American Association for Accreditation of Laboratory Animal Care (AAALAC). It is the responsibility of every employee or any other person working on behalf of Pacira at all sites studying animals to comply with the following policy:

- R&D activities will only utilize animals when there is an expectation that the results will contribute to the preservation or improvement of human health. Scientific merit, legal and ethical rationale, as well as scientific rigor and integrity, must be established before the use of animals will be authorized.
- Before authorizing the study of animals, our Chief Medical Officer will weigh the requirements for the use of animals against potential animal welfare concerns.

- Studies involving animals must meet the principles of the “three R’s” of animal experimentation: Replacement, Reduction, and Refinement. Animals will be studied only in the absence of acceptable alternatives to obtaining an identical result (Replacement); by using the smallest number necessary for the integrity of the R&D activity (Reduction); and under conditions that optimize animal welfare and prevent animal pain or distress (Refinement).

- External partners must comply with animal welfare laws and commit to the spirit of our policies. All external partners must obtain external accreditation of their testing facilities and provide updates to Pacira in any event of animal mistreatment as it occurs. To the best of our knowledge, none of these external partners use transgenic or genetically modified animals. We reserve the right to audit any external partners who perform animal research services on our behalf.

Study Registration and Publication of Clinical Trial Results

Pacira is committed to providing updates to the medical community on our R&D activities. We believe that transparency into clinical studies builds trust with the public and the medical community and helps to advance developments in public health and medical science.

All Pacira-sponsored studies that meet the definition of an applicable clinical trial are registered at, and have their results posted to, www.clinicaltrials.gov (and/or EudraCT if applicable to the study).

Additionally, the presentation of the results of our clinical trials at scientific conferences or the publication of such results in peer-reviewed scientific journals helps to ensure transparency, enables critical review by the scientific community, and advances medical knowledge. As such, we are committed to present the results of such studies at scientific conferences and submit such results for publication in peer-reviewed journals.