

Product Lifecycle Management in the Pharmaceutical Industry

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Product Lifecycle Management in the Pharmaceutical Industry

Pharmaceutical and biopharmaceutical companies are under severe pressure to improve product pipelines, accelerate time to market, and improve margins on existing products—while maintaining strict adherence to quality principles and regulatory requirements.

EXECUTIVE OVERVIEW

Pharmaceutical and biopharmaceutical companies are under severe pressure to improve product pipelines, accelerate time to market, and improve margins on existing products—while also maintaining strict adherence to quality principles and regulatory requirements. However, drug development is a long process with significant risks, and pharmaceutical companies are faced with intense competitive pressures and patent expirations that threaten profitability.

This paper discusses how a comprehensive product lifecycle management (PLM) solution can help drug companies address these business challenges and increase revenue, enhance profit, and reduce the risk of noncompliance.

INTRODUCTION

Pharmaceutical and biopharmaceutical companies often seek remedies to their challenges through point solutions. Oracle believes that pharmaceutical and biopharmaceutical companies solve their issues most effectively by implementing solutions based on a PLM philosophy. Product lifecycle management focuses on helping organizations leverage their discovery and research and development (R&D) efforts to develop new disease therapies and move them through all functions of an organization to get them to market quickly, profitably, and in compliance. A PLM approach also provides a drug company with the platform to manage change as the product moves through its useful economic life.

Choosing niche solutions that only address one portion of the drug lifecycle might actually cause more problems, because the solutions do not take into account other aspects of managing the drug through its entire lifecycle. For this reason, Oracle has created a platform of PLM solutions that enable pharmaceutical companies to deliver high-quality products to market faster and keep total product cost lower than the competition—while maintaining compliance with regulatory requirements.

By using Oracle's Agile Product Lifecycle Management solutions, pharmaceutical companies can ensure that a lifecycle approach is used in products across the R&D network as well as the extended supply chain. Specifically, Agile Product Lifecycle Management helps drug companies improve performance by

- Accelerating new drug development, introduction, and commercialization
- Prioritizing new product development and introduction
- Managing collaboration with external supply and service networks
- Providing a change management platform
- Enabling complete packaging and label management
- Facilitating regulatory submission preparation and communication
- Providing a closed-loop corrective and preventive action system
- Reducing direct material and operating costs

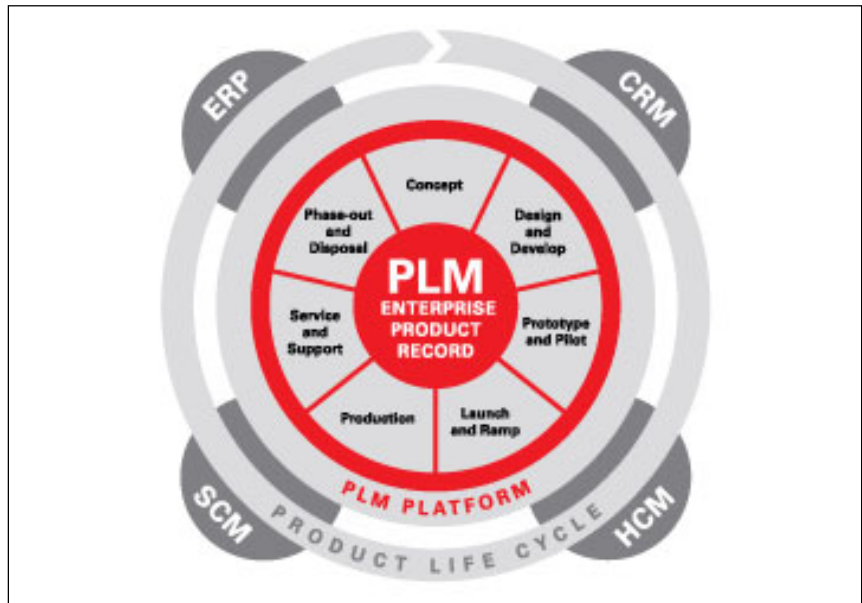


Figure 1: Agile Product Lifecycle Management is the repository for the enterprise product record.

THE PHARMACEUTICAL INDUSTRY AT A GLANCE

Drug development is a difficult process—with significant risk. The investment required for individual drug development is approaching 10 to 15 years and US\$800 million,¹ while only a fraction of the compounds in preclinical testing actually make it to clinical trials and are approved for patient use. Despite these challenges, the pharmaceutical industry has thrived, with major pharmaceutical breakthroughs leading to significant benefits for healthcare worldwide, including increased life expectancy, decreased infant mortality, reduced disability rates, and continual progress against many diseases.

¹ *Outlook 2002*, Tufts Center for the Study of Drug Development.

“The case for product lifecycle management in the pharmaceutical industry is clear... Besides the obvious faster time to market benefits, pharmaceutical supply chains have easy opportunities that surface when a manufacturer implements a PLM strategy that streamlines and rationalizes operations and products.”

—Roddy Martin,
Vice President and General Manager,
AMR Research

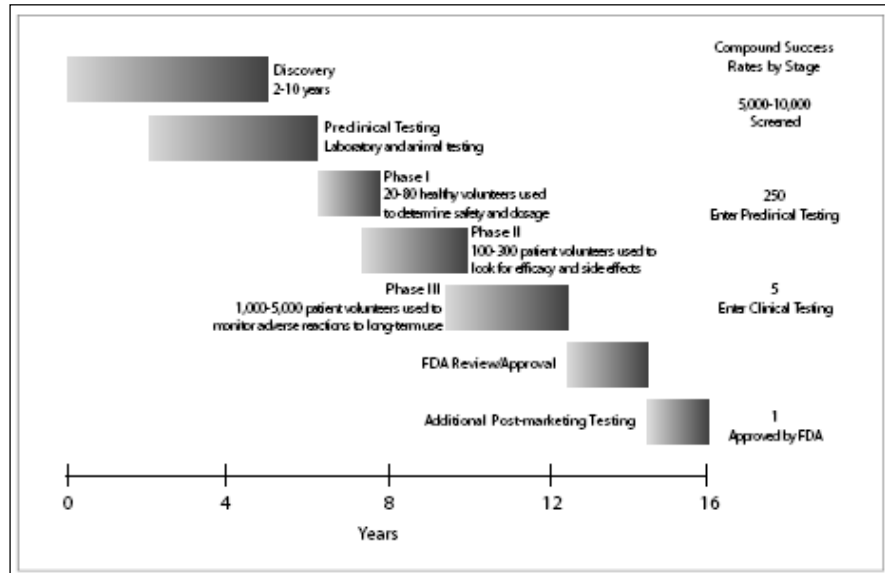


Figure 2: Bringing a successful drug to market can require up to 15 years of investment. (Source: PhRMA, based on data for the study of drug development, Tufts University, 1995.)

However, the landscape is rapidly changing and drug companies are under intense pressure to improve product pipelines, accelerate time to market, and improve margins. Today, the pharmaceutical industry is facing

- Increased competition from generics
- Patent expirations that will reduce revenues
- Small product portfolios that rely too heavily on blockbuster drugs
- Unrealized benefits from consolidation, because megamergers have not led to economies of scale or provided improvements in pipeline development
- Increased reliance on a complex network of contract service providers
- Heightened regulatory complexity



Figure 3: The pharmaceutical industry is facing many business challenges today.

To maximize profitability, pharmaceutical companies must

- Accelerate new drug development, introduction, and commercialization
- Supplement the pipeline through partnerships and licensing agreements
- Allocate R&D resources effectively by improving the ability to eliminate poor candidate compounds early
- Collaborate efficiently with partners to accelerate innovation, reduce product and process costs, and mitigate noncompliance risks
- Reduce the pain and cost of achieving regulatory compliance
- Manage effectively the change to products, packaging components, and processes
- Outsource without losing visibility and control of costs and risks across product lines and partners
- Cut direct material and operating costs
- Minimize the cost of managing product variations and extensions

Agile Product Lifecycle Management solutions assist a pharmaceutical company in delivering high-quality products to market faster and at lower cost than the competition, while maintaining compliance with regulatory requirements.

Oracle’s experience in working with pharmaceutical companies shows that these individual goals can be achieved most efficiently and effectively by adopting a PLM philosophy. This approach helps companies organize and establish business processes to streamline their discovery, R&D, and manufacturing efforts to develop new disease therapies and move them through all stages of a drug’s useful economic life. Agile Product Lifecycle Management solutions assist a pharmaceutical company in delivering high-quality products to market faster and at lower cost than the competition, while maintaining compliance with regulatory requirements.

“[A PLM] strategy represents a breakthrough opportunity to improve IT productivity because PLM’s logical focus is on what really matters to the business—finding new products and taking them through all of the functions in an organization to get them to market as quickly as possible.”

**—Roddy Martin,
Vice President and General Manager,
AMR Research**

Agile Product Lifecycle Management is a single environment for managing product portfolio information. Agile Product Lifecycle Management solutions address the key phases of the drug lifecycle and the business processes at each stage.

ADOPTING PRODUCT LIFECYCLE MANAGEMENT

Information is a research-based organization’s most valuable asset. Simple automation often gives them more data; however, that does not immediately translate into more-informed decisions during the lifecycle of a specific drug. This is especially important to pharmaceutical companies because removing even a single day from the development and regulatory approval process can pay huge dividends, providing close to US\$2.7 million in sales per day for blockbuster drugs.²

Despite efforts to improve, centralize, and automate business process infrastructure, the asset most likely to improve the decision-making—product information—remains largely unmanaged. Efficient management and effective use of the product information is critical for a company and its partners to maximize product profitability. Being able to aggregate and analyze all elements of a given compound or drug from a central location allows pharmaceutical companies and their partners to quickly address industry challenges, such as synchronizing product collaboration and overall change management.

Product lifecycle management creates a strategic framework for making informed decisions through the discovery, preclinical, clinical, regulatory approval, and full commercialization processes. This framework enables companies to have a high level of visibility and collaboration across the many internal and external functions and decision points necessary to manage a drug for optimal profitability throughout its lifecycle. When effectively managed, PLM can end the traditional isolation of the various functional teams and eliminate many time-consuming manual, paper-based change management, tracking, and approval mechanisms while providing central visibility and control over programs, costs, and schedules.

Agile Product Lifecycle Management is a single environment for managing product portfolio information. It provides visibility and control, allowing instant access to program information such as progress on deliverables and allows for optimal resource allocation. Agile Product Lifecycle Management solutions address the key phases of the drug lifecycle and the business processes at each stage.

Phase 1: Discovery

- Identify new drug targets and high-quality drug candidates
- Leverage previous research and intellectual property
- Use collaborative research networks

Phase 2: New Product Development

- Manage patent applications
- Manage clinical production processes

² Philip Needleman, “From a Twinkle in the Eye to a Blockbuster Drug,” *Research-Technology Management* 1 Nov. 2001: 38–41.

- Collaborate on and corroborate clinical trial results
- Prepare and peer review internal results reports
- Leverage preferred contract research organization (CRO) identity

Phase 3: Regulatory Submission and Approval

- Aggregate documentation for regulatory submission and archiving
- Manage nondisclosure agreement submittal and approval process
- Manage facilities inspection process
- Prepare for technology transfer

Phase 4: Product Launch

- Coordinate sales, marketing, production activities to hit launch date
- Execute technology transfer
- Gear up for new product supply

Phase 5: Commercialization

- Manage full-scale production, packaging, and labeling
- Rely heavily on chief medical officers (CMOs) and chief pharmaceutical officers (CPOs)
- Maintain current Good Manufacturing Practice process and documentation compliance
- Manage direct material costs including packaging and labeling

Phase 6: Quality Management

- Maintain and manage standing operating procedures (SOPs) and quality assurance (QA) systems
- Conduct continuous internal and external supplier audits
- Execute continuous closed-loop corrective and preventive action (CAPA) management

Phase 7: Phase-Out and Extension

- Prepare to battle generic competition
- Prepare for drug line extensions
- Continue maintenance of documentation in case of adverse events

Leveraging the Intellectual Property Portfolio

Compound UK-92480 is perhaps one of the most famous examples of portfolio redirection—by accident. Now marketed as Viagra, this compound was originally investigated as an antihypertensive. When it failed to demonstrate efficacy in clinical trials, the compound was nearly scrapped, if not for an observant clinical investigator who noted an unusual side effect.³ Nearly 10 years after that compound discovery, Viagra was approved for use in the treatment of erectile dysfunction. If the manufacturer had redirected Viagra’s crucial intellectual property earlier in the process, additional time under patent would have been preserved.

A significant amount of the time under patent protection for a new drug is typically consumed in clinical trial and regulatory approval phases. Patent protection has been further complicated by legislation such as the U.S. Hatch-Waxman Act, which contains provisions for both fostering generic competition and permitting patent owners to recover time lost during the FDA approval process.

While the Hatch-Waxman Act allows patents on pioneer drugs to be extended for up to five years, the industry still faces the prospect of losing revenue of US\$35 billion over the next five years due to patent expirations. To remain competitive, pharmaceutical companies must bring a portfolio of new drugs and drug extensions to market more quickly to take advantage of the patent protected period.

Also crucial to portfolio management is enhanced visibility across the entire pipeline because companies are integrating drug candidates from internal discovery programs with initiatives from biotech companies and CROs. Recent mergers have also created potential overlap in portfolios, as well as tremendous opportunity to reuse or redirect projects to focus on product extensions or disease platforms.

Agile Product Lifecycle Management enables companies to successfully drive their pipeline by providing critical and transparent program management capabilities. By having a centralized view of their pipeline, pharmaceutical companies can create schedules, define deliverables and owners, and link product information to different phases of the program. Team members throughout the organization and across partners can access and share critical knowledge, update project status, raise and resolve issues, and track program costs. Agile Product Lifecycle Management helps portfolio managers improve visibility and control over their pipeline to focus R&D resources on the most promising drug candidates.

Agile Product Lifecycle Management provides critical program management capabilities so companies can successfully drive their pipeline. With a centralized view of the pipeline, pharmaceutical companies can create schedules, define deliverables and owners, and link product information to different phases of the program.

³ Jim Kling, “From Hypertension to Angina to Viagra,” *Modern Drug Discovery*, Nov/Dec 1998: 31, 33–34, 36, 38.

Increasing Visibility and Mitigating Risk

Pharmaceutical and biopharmaceutical companies must create, maintain, and secure the “golden” recipe for their drugs in the master batch record (MBR). Very often the paper-based management of the MBR reduces the ability to move the drug quickly through the next phase due to extended change cycle times.

Also, key scientific personnel usually end up wasting valuable time in endless change control meetings, circling their buildings, or seeking approval signatures. Finally, security concerns and inefficiencies must be addressed, even in systems that vault and manage Microsoft Word or Adobe PDF documents.

Agile Product Lifecycle Management allows companies to structure their MBRs in a hierarchical system, linking all the MBR components, including ingredients and formulation process steps, with associated files such as SOPs, artwork, labels, packaging designs, and images.

Users easily view previous and pending revisions to the MBR via role-based access control privileges. Users with appropriate privileges can also then view, print, or check out associated documents as well as all logged and audited change history and sign-offs. All the pertinent information about the product is online and easily accessible, allowing full audit trails that are easy to review by all users with the proper authority. Many existing Oracle customers have commented that during audits, their regulatory bodies were impressed with the ease of maintaining and accessing change history.

Managing Complex Collaborative Outsourcing Networks

As industry consolidation and market pressures continue to squeeze product margins and market windows, pharmaceutical companies must rely more heavily on contract service providers to maximize efficiencies, focus on core strengths, and leverage the collective expertise of their partners. Agile Product Lifecycle Management provides secure, distributed, role-based access to critical product information to all appropriate constituents. Its collaboration capabilities bring together the knowledge and skills of all appropriate resources—both internal and external—to quickly identify product and process issues as well as recommend, approve, and enact changes to solve the issues. It allows companies to initiate and approve changes driven by manufacturer, customer, and supplier. The quicker an enterprise can publish change data to appropriate parties, the faster and more effectively they can implement change and manage costs.

Agile Product Lifecycle Management allows companies to structure their MBRs in a hierarchical system, linking all the MBR components, including ingredients and formulation process steps, with associated files such as SOPs, artwork, labels, packaging designs, and images.

Agile Product Lifecycle Management ensures that the parties in the network have secure, role-based access to critical product information. It allows companies to initiate and approve changes driven by manufacturer, customer, and supplier.

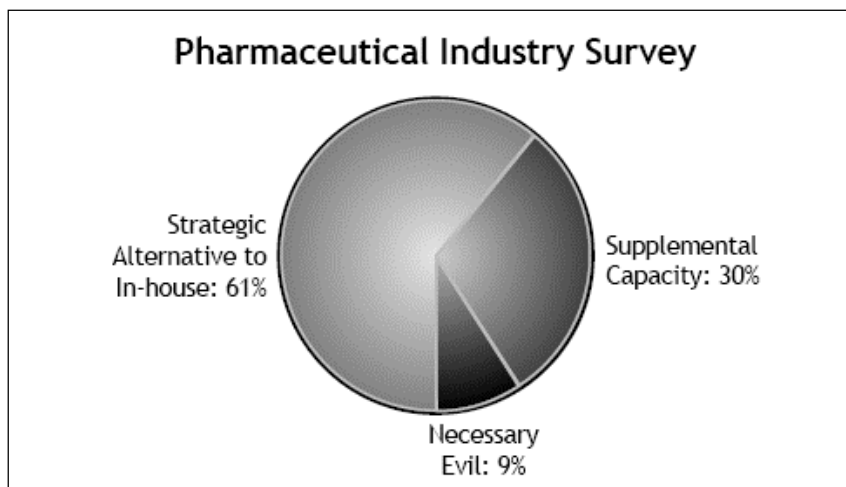


Figure 4: “How would you characterize your company’s attitude toward outsourcing?” (Source: “Survey Reflects Growing Maturity of CMC Outsourcing,” *PharmTech*, Aug. 2002.)

Companies can remotely review and approve outsourced portions of products and projects by sharing data with their product development organizations, contract research organizations, CMOs, and CPOs, using Product Definition eXchange (PDX). Analogous to an electronic overnight delivery service, PDX enables real-time transfer of electronic files with the ability to maintain document priority and electronic approvals. PDX uses the industry standard product information format based on Extensible Markup Language (XML) technology to maintain U.S. FDA Code of Federal Regulations (CFR) Part 11 compliance via audit trails, validation, and electronic signature validation. (For more information about PDX, please visit www.pdxstandard.org.)

Managing Packaging and Labeling

The costs associated with drug discovery and development are well documented. Once in commercialization, however, packaging can represent up to 75 percent of the cost of a manufactured drug.

Pharmaceutical packaging is highly regulated and must focus on product safety, integrity, and ingredients as well as adverse event labeling. International distribution also forces pharmaceutical companies to address multiple regulatory and language requirements, as well as counterfeit controls. Estimates are that 30 to 40 percent of all pharmaceutical product recalls are due to labeling and packaging issues.

In today’s highly competitive environment, controlling costs and maintaining maximum flexibility is vital to a drug’s commercial success. Using Agile Product Lifecycle Management, companies can maintain visibility and control over multiple label designers and printers as well as synchronize global production and packaging operations, while maintaining compliance with common manufacturing principles.

Agile Product Lifecycle Management empowers organizations to manage and lower costs throughout a drug's lifecycle. It increases the value of supply network information and relationships to ensure total cost targets are optimized.

Reducing Product Cost

Agile Product Lifecycle Management empowers organizations to manage and lower costs throughout the lifecycle of a drug. Drawing from multiple tiers of the supply chain, it obtains forward-looking market information, such as prices and lead times, to enable product management and sourcing or procurement organizations to reduce prices and material costs. It allows efficient cost rollups (including nonmaterial costs), future product cost variability, and global cost management. Agile Product Lifecycle Management also leverages an approved vendor list to ensure quality and total cost targets are optimized.

Managing Closed-Loop Corrective and Preventive Action Systems

With the responsibility for delivering a high-quality product, many pharmaceutical companies have found it necessary to implement additional quality management systems. To achieve compliance with corrective and preventive action (CAPA) requirements, companies need an infrastructure to detect existing or potential quality problems, quickly get to the core issue, and swiftly implement resolution.

Agile Product Lifecycle Management delivers a first-of-its-kind, complete closed-loop CAPA process that enables pharmaceutical companies to reduce quality variability and decrease quality assurance administrative costs. Having CAPA procedures online and tightly integrated with core product information reduces costs by eliminating manual documentation requirements, expensive communication errors, and lengthy feedback procedures.

Agile Product Lifecycle Management not only provides integrated processes to drive quality variation information back into R&D and manufacturing operations, but also provides collaborative workflows to ensure that problems are quickly corrected. Through rapid identification, analysis, and correction of issues, companies can increase quality and improve both their bottom line and competitive position. With Agile Product Lifecycle Management, enterprises will be able to continually improve the product based on feedback from customers; employees; suppliers; distributors; and contract research, contract manufacturing, and contract packaging organizations.

ENABLING FEDERAL COMPLIANCE

Agile Product Lifecycle Management enables customers to meet all requirements of Title 21 of the U.S. FDA Code of Federal Regulation (CFR) Part 11, which prescribes the accepted use of electronic records and signatures. Agile Product Lifecycle Management captures all comments and approvals associated with changes executed within the solution. These records contain the electronic signatures, comments, and justification for the changes as well as form an audit trail that completely addresses the Part 11 requirements.

Oracle and validation partner U.S. Data Management have provided the FDA with an overview of Agile Product Lifecycle Management solutions and their role in helping life sciences companies bring new products to market while maintaining

compliance with FDA regulations such as 21 CFR Part 11. Discussions focused on the nature of electronic documents and how the use of Agile Product Lifecycle Management could potentially improve communications between the FDA and industry. Oracle reviewed the management of electronic documents, including security and access control, electronic signatures, and validation approaches. In addition to addressing the appropriateness of representing Agile Product Lifecycle Management as Part 11 compliant, the discussion focused on potential applications for use of the software by FDA field investigators.

LIFTING THE BURDEN OF SYSTEMS VALIDATION

The FDA requires validation of all software used as part of the quality system of any life sciences company. The agency also wants to ensure the software will perform as it is intended for its chosen application. Developing validation plans, protocols, and executing them can be a time-consuming and expensive task. Often the cost to validate a system is as much or more than the system itself. Oracle offers a suite of protocols that customers can use in their validation effort.

Oracle understands that pharmaceutical and biopharmaceutical companies are under intense FDA scrutiny and that the cost to validate a computer system can be more than the system itself. Oracle has contracted with a recognized, independent third-party firm to develop a suite of test protocols. This enables customers to review and approve a validation plan, execute the protocols, and document the results, thereby reducing the need for expensive consulting engagements.

Oracle's Agile Food and Drug Administration Validation Pack is ready out of the box. It helps customers meet all regulatory guidelines around system validation and was recently reviewed by the FDA. The Agile Food and Drug Administration Validation Pack contains the following:

- Master Validation Plan
- Installation Qualification
- Operational Qualification
- Performance Qualification
- Traceability Matrix
- Final Validation Report

“We are pleased with the positive response received from the FDA on the collaboration of Oracle's best-of-breed Agile Product Lifecycle Management solutions and USDM's compliance and regulatory expertise. Oracle and USDM are committed to offering the life sciences industry premium PLM solutions, focusing on regulatory compliance.”

**—Melissa Allensworth,
U.S. Data Management**

CONCLUSION

According to a recent AMR Research report, Agile Product Lifecycle Management's customer reference scoring included "evaluation of use volume, difficulties associated with implementation and upgrading, ability to integrate with other applications, complexity of implementations, depth of use, and level of satisfaction with Agile [Product Lifecycle Management's] suite of products."

In the same report, Agile Product Lifecycle Management was ranked highest for customer satisfaction and direct materials sourcing functionality and higher than the industry average in PLM functionality.⁴

The ability of Agile Product Lifecycle Management to centralize and manage product information helps pharmaceutical companies leverage their investment in information technology and PLM processes. The Agile Product Lifecycle Management platform is designed to address pharmaceutical companies' most pressing business issues including speeding time to market, reducing operating and product costs, achieving high-quality standards, and providing product governance and compliance with regulatory agencies.

The flexible architecture of Agile Product Lifecycle Management enables the applications to be delivered "business-ready" to pharmaceutical companies. Highly configurable, Agile Product Lifecycle Management solutions do not need long implementation cycles requiring custom programming to tailor a solution to a particular company. Kevin O'Marah, vice president of AMR's PLM Research writes, "[Oracle's] Agile [Product Lifecycle Management] clients had the highest level of satisfaction in terms of product performance and capabilities, sales experience, and service and support provided during the implementation and upgrading."

⁴ Kevin O'Marah, "Product Lifecycle Management: What's Real Now," AMR Research, September 2002.



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Oracle Corporation
World Headquarters
500 Oracle Parkway
Redwood Shores, CA 94065
U.S.A.

Worldwide Inquiries:
Phone: +1.650.506.7000
Fax: +1.650.506.7200
oracle.com

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