

Professional Qualifications Pharmaceuticals



Engineering | Architecture | Construction | Consulting



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Firm Overview



Firm Overview



Design, construction and consulting solutions for life sciences and advanced technologies.

Engineering

Across disciplines, across industries, engineering expertise creating successful solutions.

Architecture

Thoughtful, collaborative and insightful designs inspiring facilities that integrate form with function.

Construction

From start-up to the finish, delivering safe, reliable and efficient advanced technology facilities.

Consulting

Strategic business thinking, technical expertise and hands-on experience improving success.







Firm Overview



Every day, the CRB team shows the world what makes us most unique as a company: our relentless pursuit of success for our clients.

CRB is a global design, construction, and consulting firm that relentlessly pursues and delivers success for our clients in advanced technology industries. Founded in 1984 as a single three-person office, we have grown to a team of more than 1,000 passionate professionals in 15 offices. CRB's single-minded focus on putting our clients' interests first – every day, on every project – defines us as a firm.

Structured to Serve

CRB understands that not only is each client unique, but the scale and needs of each project are as well. This is why our broad-based firm has been strategically structured to offer a comprehensive portfolio of services on any project. From architecture and engineering to construction services and operational consulting, we customize our offerings to fit each client's unique needs, requirements, and business goals, helping them succeed in their respective advanced technology markets.

Our network of technical experts takes an adaptive, tailored approach to each project, so that clients always receive the best, most economical solution. This may mean individual selections from CRB's architecture, engineering, construction, and consulting practices, or our ONEsolutionTM offering, which provides end-to-end integration and complete project oversight. As a firm of notable breadth, we are able to customize our services by scaling up or down, based entirely on what a client needs to be successful.

Our clients require buildings that provide a wide range of outcomes to support their institutional goals. CRB focuses on delivering facilities that reach beyond bricks and mortar and deliver measurable outcomes integrated with our client's strategic mission.

Experts in Advanced Technology

We have developed an international reputation for providing architectural, engineering and construction solutions for advanced technology industries. In fact, 90 percent of CRB's projects come from this industry, with top private and public institutions consistently turning to CRB for our deep knowledge of how to plan, design, and build facilities of this kind. Through work on hundreds of projects, we have an unparalleled understanding of how to equip scientists and other professionals with efficient, flexible, and interactive work environments that can lead to successes

From Concept Through Completion

CRB delivers in all areas of project execution, from strategic planning and initial project programming, through conceptual and detailed design and into construction, commissioning, and validation. From concept through completion, we contribute innovative ideas and cost-effective designs and services, ensuring that projects are realized on time and on budget.

What We Value, What We Promise

CRB's extraordinary growth over the past three decades has been fueled by our core values and promises: Unrivaled passion for seeking out the right solution on every project; deep technical expertise to tackle the toughest challenges; a company structure built on collaboration and empowerment; and people with integrity and purpose who advance our industry and help our clients make the world a better place.



Awards

As an internationally recognized firm, CRB has been the proud recipient of multiple awards, including the coveted ISPE Facility of the Year Award. CRB was also the first-ever professional services provider to receive the ISPE Company of the Year Award in 2001, an accolade that was repeated in 2012. CRB's most recent awards are featured below:

2018 ISPE Facility of the Year, Facility Integration Los Angeles Building 8 Shire, California

Building 8 was a 120,000-square-foot purification facility integrated into an 11.6acre campus with eight other buildings and space constraints on all sides.

2018 ISPE Facility of the Year, Project Execution Project FAITH BioMarin Pharmaceuticals, California

Project FAITH converted an office and warehouse building into an 18,000- squarefoot gene therapy facility. It was one of the first gene manufacturing facilities of its kind in the world.

2018 ISPE Facility of the Year, Operational Excellence

Los Angeles Quality Control Lab Shire, California

Relocation of a 16,000-square-foot quality control lab ensured better, faster and more economical delivery to patients, allowed for future expansion and decoupled the lab from manufacturing operations and infrastructure.

2018 ISPE Facility of the Year, Honorable Mention BARDA-CIADM Facility Expansion Emergent BioSolutions, Maryland

This project was a unique partnership between industry and government to rapidly deploy development and manufacturing capabilities in response to a global pandemic. The steel-framed, three-story expansion doubled the size of the existing 56,000-square-foot building. This Center for Innovation in Advanced Development and Manufacturing is one of three such facilities in the United States.

2017 ISPE Facility of the Year, Facility Integration Clinical Manufacturing Building

Bristol-Myers Squibb, Massachusetts

This 131,000-square-foot multistory facility provided for the manufacture of late-stage clinical and commercial-launch supply of biologic bulk drug substance. The initial build-out provided a nominal bioreactor capacity and housed office space, a just-intime warehouse, process utilities, weigh and dispense operations, solution prep and parts wash/sterile prep.

2017 ENR Regional Best Projects, Award of Merit, Manufacturing 2017 ENR Best of the Best Large-scale Manufacturing 3X Capacity

Upgrades Biogen, North Carolina

This design-build manufacturing project included deconstructing seven specific manufacturing areas totaling over 100,000 square feet and rebuilding the seed train bioreactor suite.

2015 ENR Regional Best Projects, Award of Merit, Manufacturing Innovation & Manufacturing Facility

Herbalife, North Carolina

This design-build renovation of a 792,000-square-foot facility that manufactures nutritional supplement powders, liquids and teas was honored as one of the best construction projects in the Southeast.







FOYA 20 Facility of the Year Awards CATEGORY WINNER













Awards

2015 Plant of the Year

Greenfield Confectionery Facility Mars Chocolate North America, Kansas

This LEED Gold certified project was recognized as the most innovative new food or beverage plant built in North America by Food Engineering magazine.

2014 ENR Regional Best Projects

Lab/Office Expansion Agilent, Colorado

The recipient of many awards, this project was designed in a phased, multi-year approach. CRB delivered the design-build project on time and on budget, despite severe floods in 2013.

2013 ISPE Facility of the Year, Facility Integration

Flexible Volume Manufacturing Biogen Idec, North Carolina

Designed to be fully upgradable to ISO-7 and ISO-8 classified spaces, this facility demonstrated that closed systems can be maintained throughout the entire manufacturing process.

2013 ISPE Facility of the Year, Process Innovation GMP Warehouse Novartis, North Carolina

An EPCM approach was used to adhere to the aggressive schedule to complete this greenfield manufacturing facility that integrated fill/finish innovation, labs and administrative space.

2012, 2001 ISPE Company of the Year

This award honors companies that continually support ISPE's commitment to providing knowledge and best practices to help meet technical challenges of the pharmaceutical manufacturing industry.

2011 KC ASHRAE Technology Award

Venture Lab Accelerator Kansas Bioscience Authority, Kansas

This LEED Gold certified project included

unique sustainability features, such as a lake water heat exchanger, natural gas generator and 55 percent reduction in energy use from ASHRAE's baseline standard.

2011 ISPE Facility of the Year, Honorable Mention, New Technologies Project Atlas Shire HGT, Massachusetts

A biological manufacturing facility, Project Atlas incorporated first-in-kind disposable technology and a first-in-kind 2000-liter single-use bioreactor.



















Single Resource for Clients





ONEsolution[™]

CRB's ONEsolution integrates planning, design and construction into a structured, measurable and efficient approach to achieve your project objectives with a single, accountable entity. From concept to completion, our integrated, multidisciplinary process allows for innovation and efficiency in achieving your project goals.





ONEsolution

Single Team, Common Goals

CRB's ONEsolution provides you with a single source of responsibility, communication and streamlined coordination. From start to finish, CRB's planning, design and construction professionals are aligned with your vision and driven to collectively pursue and achieve your goals for success.

Early Reliable Cost, Reduced Risk

Today's traditional architect/engineering/construction management delivery model can be a challenge to manage because it often ends with unpredictable results and financial risk. Rather than budgeting to your design, CRB's design and construction team gains a deep understanding of your facility requirements and then designs to your budget and needs. Your risk is minimized with an early cost projection and predictable results.

Schedule Optimization

The early collaboration of CRB's planning, design and construction team allows for complete awareness of project goals and utilization of expertise across all disciplines. Resources are maximized, schedules are optimized and redundancies are eliminated, allowing your project to move forward with streamlined consistency. Compared to industry averages, our request for information and shop drawing turnaround time is 15 percent faster, and the total cost of rework is significantly less. Many projects have reduced project delivery time by more than one-third compared to industry standards.

Value from Concept to Completion

Through our commitment to lean design and construction principles, CRB eliminates waste and identifies innovative, costeffective solutions to maximize value for your project. CRB deploys the latest virtual design and construction technology to optimize efficiencies throughout your project's life cycle.

Single-source Accountability

ONEsolution provides seamless collaboration between you and our design, construction and commissioning and qualification professionals. By removing the traditional trade boundaries and layers of responsibility, sound judgments that transform your vision into reality can be made. There are no handoffs, priorities lost in translation or finger pointing-removing inefficiencies and the stress of your decision making.

Development and Adherence to the Project Quality Plan

From the start of your project, CRB's integrated team collaboratively works to meet performance needs, not just minimum requirements, providing innovative solutions that can often deliver a better facility than initially imagined. Our design and construction professionals work hand in hand to develop the design while projecting costs through the conceptual, design development and construction phases.

CRB's Safety Program

ONEsolution enables an increased knowledge of your project's workflow across our design and construction team. Our Environmental, health and safety program adopts a "zero accidents" policy toward safety management and requires us to operate in a manner protective of our employees, partners and the environment. You can be confident in relying upon a single source that possesses one of the leading safety records in the industry.

The strong combination of design and construction professionals on this team was undoubtedly the key in executing this very complex project in the shadow of an extremely aggressive schedule.

> Facilities Engineer, Ceva Biomune



Subject Matter Experts



Subject Matter Expertise

What is CRB's greatest differentiator? The people! Our worldclass technical experts are motivated by new challenges and have both the experience and inspiration to create custom solutions to fit your needs.

Technical Excellence

CRB people are in constant pursuit of learning, sharing and providing world-class technical excellence. And while we can be innovative and forward thinking, we believe first and foremost to provide the RIGHT solution to meet our clients' technical needs.

Industry Guidance Document Contributions

For two decades, CRB's thought leaders have been involved in the development of Pharmaceutical industry Standards, including the authoring and co-authoring of ISPE Baseline Guides. Working regularly with industry leaders, peers, regulators and compliance specialists has enabled CRB to gain unparalleled knowledge of the regulatory trends and standards that shape the future of facility design.

Our subject matter experts are sought-after speakers and authors, providing insights on the technical challenges affecting advanced technology clients today and in the future. We are proud to contribute to the best practices that deliver cost-effective, safe and successful solutions for our clients and the industry.

Additional Industry Document Contributions and Participation Include:

- ASME BPE authors
- Biotechnology Industry Organization (BIO) contributors
- BioPhorum Operations Group (BPOG) contributors
- American Institute of Architecture (AIA)
- Parenteral Drug Association (PDA)
- International Institute for Sustainable Laboratories (I2SL)
- ASHRAE
- Tradeline
- TurnKey





Services & Capabilities



Pharmaceutical



The finished pharmaceutical, nutraceutical and chemical industries have become increasingly sophisticated. Intense competition has placed growing pressure on companies to get their products to market as quickly and efficiently as possible. Facilities that seamlessly incorporate production, filling, packaging and distribution are critical.

CRB has assisted pharmaceutical companies in responding to market conditions and reaching their business goals through innovative, insightful, sustainable solutions. CRB understands that the increased productivity and minimized waste of a successful manufacturing facility is achieved through plant design that offers optimal flexibility and easier validation.

We offer design and construction experience from bulk pharmaceuticals, nutraceuticals and chemicals to finished manufacturing. Our finished manufacturing experience includes parenterals, tablets, liquids, creams and ointments.

Whether you want to upgrade your process utilities or build a new manufacturing facility, we will listen to your needs and deliver the solutions you require in this fast-paced market.

Our pharmaceutical teams include knowledgeable consultants who have been in your position, thought leaders who lend their talents to the advancement of the pharmaceutical engineering field and dedicated professionals who have gained experience from hundreds of pharmaceutical projects around the world. CRB understands your challenges and can provide planning, design and construction solutions tailored to meet your business objectives.

The right solutions for your pharmaceutical business:

- Operational technologies/specialty markets
- Oral solid dosage
- Fill/finish design
- Aseptic processing
- Packaging
- Strategic facility planning
- Sustainability
- Operations improvement
- ONEsolution™



Pharmaceutical

Whether you need a partner to design a facility expansion, renovate or retrofit a legacy facility, consolidate your master planning or maximize the capacity and efficiency of your current operations, you can count on us to relentlessly pursue and deliver the right solutions for your project.

Representative Pharmaceutical Clients

AB BioTechnologies Inc.	DPT Laboratories	Medrad	
Abbott	Dr. Reddy's Laboratories	Mentor Corp.	
Agensys	DSM Pharmaceuticals Inc.	Merck & Co.	
Alcami Corp.	Eisai Co.	Meridian Medical Technologies	
Alcon	Elanco	Metrics Contract Services	
Alexza Pharmaceuticals	Eli Lilly and Co.	Millipore Sigma	
Allergan	Emergent BioSolutions	Nature's Way	
AlphaVax Inc.	Endo Pharmaceuticals	Nektar Therapeutics	
Amerigen Pharmaceuticals	Enzon Pharmaceuticals	Neutrogena Corp.	
Amgen Inc.	Ethicon Inc.	Noramco	
Amneal Pharmaceuticals Inc.	Fibrocell Science	Novartis	
Amway	First Boston Pharma	Pacira Pharmaceuticals	
Aptuit	Gallus BioPharmaceuticals	Patheon Inc.	
Aquestive Therapeutics	GE Healthcare	Perrigo Co.	
Ash Stevens	Gilead Sciences Inc.	Pfizer Inc.	
Astellas Pharma US	GlaxoSmithKline	Pharmavite	
AstraZeneca	Hisamitsu Pharmaceutical Co. Inc.	Procter & Gamble	
B. Braun	Hitachi	PuraCap Pharmaceuticals	
Bausch + Lomb	Hospira Inc.	Regeneron Pharmaceuticals Inc.	
Baxter	Insmed Inc.	Roche	
Bayer HealthCare Pharmaceuticals	Ionis Pharmaceuticals	SAFC	
Becton, Dickinson and Co.	Ivy Laboratories	Sandoz	
BioMarin Pharmaceutical	Janssen Biotech	Sanofi	
Boehringer Ingelheim Vetmedica	JHP Pharmaceutical	Stryker Corp.	
Bristol-Myers Squibb	Johnson & Johnson	Teva Pharmaceutical Industries	
Cardinal Health	King Pharmaceuticals	The 3M Co.	
Catalent Pharma Solutions	KV Pharmaceutical Co.	Unilever Home & Personal Care	
Celgene Corp.	La Jolla Pharmaceutical Co.	United Therapeutics Upsher-Smith Laboratories	
Covidien/Mallinckrodt	LLOYD Inc.		
CSL Behring	MannKind Corp.	Valediti Fildi Indueuticais International	
Dow Pharmaceutical Sciences Inc.	McNeil Consumer Healthcare	zosano i narma oorp.	

Professional Qualifications | Pharmaceuticals



Architecture



At the forefront of each architectural project is the same objective: Develop innovative design solutions that enable our clients to enhance their competitive advantage and achieve their business/cultural goals.

CRB is an architectural leader in advanced technology markets, providing unique value-added solutions to solve clients' most complex facility challenges. Our architectural team members are specialized industry experts who embrace collaboration with our clients to create successful and modern facilities.

Collectively with our engineers, builders and external consultants, we create an integrated design approach that enables us to develop project-specific solutions that are operationally sound, fiscally accountable and environmentally responsible. Together, we leverage new building technology and materials to provide opportunities for innovation and design excellence. This collaborative approach enables us to develop exceptional, long-term working relationships with our clients.

Market Focus

- Medical devices
- Biotechnology
- Pharmaceutical
- Science + technology
- Food + nutrition

CRB offers a full range of architectural services from initial predesign strategic planning and feasibility studies through construction administration.

Pre-Design/Planning

- Feasibility studies
- Programming

- Logistical site and process master planning
- Current Good Manufacturing Practice (CGMP) gap analysis

Conceptual/Basis of Design

- Future facility and future lab design concepts
- Specialized space planning methodologies

Construction Documents

- Integrated, multidisciplinary 3-D modeling
- CGMP facility design
- Strategic code compliance solutions
- Sustainable design/ Leadership in Energy and Environmental Design
- Specifications

Construction Administration

- Bid evaluation
- Request for information response
- Submittal review/approval
- Construction observation
- Final punch list/project closeout assistance



Process Architecture



CRB delivers integrated facility design that provides elegant solutions to complex requirements of Current Good Manufacturing Practice production facilities. With a passion for achieving optimal facility solutions, our process architects approach every project with thoughtful consideration for ideal process flow, efficient utility connections and appropriate equipment access for operators resulting in a cohesive facility that is highly functional with a safe and pleasant work environment.

Process Architecture Expertise:

- Industry leadership in regulatory compliance
- Interdisciplinary collaboration
- Facility integration
- Lean, efficient flows of process, equipment, materials, waste and people
- Environmental protection and segregation of process unit operations
- Sustainability
- Flexibility
- Places for people
- Daylighting
- Visual connection
- Regulatory and code requirements for Current Good Manufacturing Practice, biosafety level and hazardous materials



Process Design

For more than 30 years, CRB's process engineers have applied their in-depth knowledge and experience to the unit operations of a wide variety of advanced technology processes. They possess a deep understanding of the technical drivers that impact the engineering solutions and success of your project.

By combining our broad range of process engineering expertise with the application of dynamic simulation techniques, we consistently provide practical design processes that operate efficiently, sustainably and economically. Our process engineers provide production solutions that are sharply focused on output, energy and safety. We are committed to helping you increase your return on investment, improve production yields and enhance capabilities.

Our process engineering capabilities include the following services:

- Process simulation
- Process architecture
- Packaging engineering/integration
- Lean design/plant optimization
- Process design and scale-up
- Super-skid and module design
- Chemical engineering
- Warehouse and material flow analysis
- Risk assessments and hazard and operability study reviews
- · User requirement specifications and equipment specifications
- Virtual design and construction/building information modeling/3-D design and isometrics
- Ergonomic studies
- Sustainability evaluations
- Turnkey solutions and project management
- Specialty contractors and installers coordination
- Factory acceptance test/site acceptance test/start-up services









Central Utilities

Planning and Design



Reliable and energy-efficient central utility operations start with sound engineering design. The right solutions include systems that are simple to operate and maintain and flexible and adaptable to meet your current and future needs. As engineers and communicators, we listen to your needs, understand your requirements and then strive to deliver solutions that meet your expectations.

Whether you are planning or renovating a central plant, CRB can provide the experience and resources that you need. Our team of experienced engineers and designers can provide you an integrated approach, through the use of 3-D modeling, to deliver your project with the end results in mind. By modeling the central plant equipment, it will enhance interdisciplinary coordination and reduce costly interferences prior to actual construction.

Energy efficiency, reliability and safety are critical factors in the operation and success of any facility. We understand that owners only spend what is necessary for utilities to support current manufacturing operations but need central utilities buildings to be designed for flexibility so that they can be expanded to meet manufacturing and facility growth plans. We can provide hydraulic modeling and piping stress analysis that result in systems that are economically sized to meet facility needs.

We provide a total service package from the planning and budget phase through design, construction and system startup. The services we provide include mechanical, electrical, plumbing, fire protection, specialty gases, clean and plant piping, instrumentation, commissioning and startup for retrofits and new facilities.

Project Management

Our goal is to provide quality engineering services in a timely manner. These goals often conflict. It is our job to understand and evaluate your objectives and priorities:

- Schedule development and tracking
- Budget development and tracking of earned value
- Project scope development and programming

Innovative Planning and Design

- Strategic utilities master planning and layout
- Interactive 3-D modeling with infrastructure clash detection
- Intelligent piping and instrumentation diagrams with integrated database management
- Due diligence/feasibility studies/life-cycle cost analysis
- Hydraulic modeling of piping systems
- Start-up and commissioning support
- Energy management optimization
- Central utility plant expansions and upgrades



Central Utilities

Planning and Design

Mechanical

- Chillers (centrifugal, absorption, reciprocating)
- Hydraulic modeling of piping systems
- Steam and hot water boilers
- Thermal storage (stratified tank, ice banks)
- Energy recovery (runaround coils, air-to-air heat exchangers, enthalpy wheels)
- Free cooling plate and frame heat exchangers

Piping, Plumbing and Fire Protection

- High purity reverse osmosis/deionized water systems
- Specialty gases (nitrogen, oxygen, argon, carbon dioxide)
- Compressed air and lab vacuum
- Piping stress analysis
- Process/sanitary waste and vent
- Storm and roof drainage
- Automatic wet and dry sprinkler systems
- Special systems (waterless fire suppression systems)

Electrical

- Low- and medium-voltage power distribution systems
- Lighting systems
- Voice, data and public address systems
- Fire detection and alarm systems
- Short circuit analysis
- Load studies and peak shaving
- Power conditioning and surge protection
- Emergency power and uninterruptible power supplies

Instrumentation and Controls

- Building control and automation planning and philosophy
- Control system architecture
- Critical equipment monitoring (freezers and incubators)
- Instrument data sheets
- Control loop diagrams
- Sequence of operation
- Single loops and relay logic
- Control system programming











Energy Optimization

Our clients have experienced a 10-20 percent reduction in utility bills with no-cost or very low-cost operational changes. In many cases, an additional 20-30 percent annual energy cost savings can be achieved under capital cost programs with payback periods of two years or less.

As is the case in most facilities regulated by the Food and Drug Administration, efforts to reduce operating costs must be mindful of operational complexity and risk to production efforts. CRB provides a comprehensive energy optimization analysis that identifies risks, defines operational requirements and works to ensure long-term performance and energy efficiency.

In existing facilities, energy auditing is the first task we perform to develop an energy optimization strategy. Our energy audit consists of a detailed examination of how your facility uses energy and the overall energy expense. We can recommend a program for changes in operating practices and energy-consuming equipment that will effectively reduce energy bill expenses and reduce emissions of environmental pollutants Our knowledge of state energy reduction programs will also enable us to reduce your initial cost investment.

FDA-regulated facilities are highly specialized and require an energy auditing team familiar with unique and complex process requirements to create an effective energy saving strategy. We have several specialists who are certified by the Association of Energy Engineers as certified energy managers. These specialists work together with our experts in FDAregulated manufacturing to perform a whole building evaluation that identifies opportunities for energy savings without compromising regulatory compliance. Our understanding of your process and regulatory requirements, coupled with energy saving expertise and energy reduction incentives, provide you with realistic solutions from an industry-specific knowledge base.

Basic Components of Energy Audit Activities:

- Collect facility operation information and utility bill records
- Analyze facility energy use
- · Identify energy saving opportunities
- Specify changes to reduce energy use (energy conservation opportunities (ECOs))
- Assess ECOs in terms of initial costs and operational savings
- Prioritize ECOs by initial cost, total operational cost savings and simple payback
- Develop an action plan for ECO implementation

We Apply:

- Sustainable principles
- Energy evaluation
- Hydraulic modeling optimization of mechanical system operation
- Energy efficiency control strategies
- Process knowledge
- Regulatory expertise
- Lean manufacturing concepts

Expected Results

- Report detailing major energy consumption
- ECO return on investment analysis
- Recommendations to reduce energy use

The Association of Energy Engineers

Since 1981, the Association of Energy Engineers has certified more than 7,000 professionals, enabling them to receive special recognition for their expertise in a variety of specialized areas of the energy industry. These certification programs are recognized by many government agencies, such as the U.S. Department of Energy and the U.S. Agency for International Development, corporations and utility and energy service companies.





Fill Finish Design



Our success is based on the process expertise we bring to our clients' projects. We combine that expertise with a strong knowledge and understanding of Food and Drug Administration requirements and system design capabilities to make your project a success.

Areas of Expertise:

Sterile Products

- Component preparation
- Formulation
- Filling
- Lyophilization
- Capping, sealing
- Terminal sterilization
- Inspection
- Labeling
- Coding
- Vision systems
- Packaging

Non-sterile Products

- Milling/blending
- Weighing
- Granulation
- Fluid bed processing

- Tablet compression
- Coating
- Filling (bottles, tubes)
- Capping
- Induction sealing
- Labeling
- Coding
- Vision systems
- Packaging
- Hands-on experience
- People, material and equipment flows
- Minimize cross-contamination, mix-ups and errors
- Delivering industry-leading engineering solutions
- Cost-effective facility that can be validated
- Compliant with governing codes, laws, regulations and your needs



Fill Finish Design

Operating and engineering design company experience with pharmaceutical fill-finish facilities enables CRB to understand and help you meet the daily challenges in producing and moving product through your facility.

Innovative layout and line design starts with listening to you and offering a customized approach that best satisfies your specific business needs.

- Application and use of barrier isolation
- Traditional filling suites
- Secondary and tertiary packaging lines
- Practical and reliable results
- Validation-oriented documentation

Engineering Services

- Facility programming and layout
- Project definition and scope development
- Process flows
- Technology selection
- Process simulation
- Line layout
- Clean-room mechanical/HVAC design
- Hazardous area design
- Process, automation and mechanical/electrical system design
- 3-D modeling
- Piping isometrics
- Detailed commissioning plans and protocols

Construction Management

• Full construction management services









Packaging



Packaging is the most visible statement you can make to your customers and your competition. Whether your goal is to efficiently introduce a new packaging component to a manufacturing facility or design new packaging production lines, CRB brings diverse expertise to your project by developing creative solutions for your project from concept to implementation and startup.

Leading companies are leveraging CRB's world-class team of packaging experts for help with their most demanding packaging and material handling challenges. We have assembled a packaging expert team with experience in a wide range of industries and production environments.

We develop a unique working relationship with each customer to support decisions that not only meet present goals but also meet future ambitions. This has resulted in relationships where we provide anything from on-site engineering services and project management for employee augmentation to full-scale projects, including new facilities and equipment. As a full-service engineering, architecture, construction management and consulting provider, we can deliver a complete turnkey project solution. You can be confident we will deliver an equipment and facility design solution that can be executed efficiently and effectively from construction through successful commercial operation.

Our engineers have extensive experience and can provide a broad range of packaging engineering services. We are proud of our ability to work in collaboration with all stakeholders-from supply chain, materials procurement, plant operations, vendors, marketing, corporate quality, packaging and research and development.

Areas of Expertise

- Packaging line design
- Packaging simulation
- Commissioning, qualification and validation
- Installation/operational/performance qualification
- Process and material flow analysis
- Packaging performance testing-lab and field
- Systems integration
- Cost analysis
- Line optimization
- Line relocation
- Labor reduction
- Capacity planning and improvements
- Line startup and debugging
- Component qualification/commercialization
- Warehouse utilization
- Inventory reduction
- Automation systems
- Material flow analysis
- Distribution study/damage reduction
- Accelerated testing
- Dosing



Packaging

Components Knowledge

We also have a broad knowledge base with a wide variety of package component types across multiple industries. We understand the relationship between components and the equipment necessary to maintain package integrity.

- Ampoules/vials
- Aseptic/modified atmosphere packaging
- Pharmaceutical bottle/blister packaging (liquid and solid dose)
- Pharmaceutical compliance packaging
- Bags/pouches/packets
- Consumer product and personal care bottles/jars
- Cans/canisters
- Cartons/cases/trays
- Caps/crowns/lids
- Pumps/dispensers
- Decorating/marking/coding
- Drums/totes/super sacks
- Grouping/ separating/bundling
- Stretch and shrink films
- Roll fed/cut and stack/shrink/pressure sensitive labels
- Kegs/casks
- Displays and promotional packaging
- Tubes/sleeves
- Adhesives/tapes
- Wood/igps/composite pallets

Materials Knowledge

We transfer our diverse materials expertise to your project by developing creative solutions. We understand the sensitivities in materials selection at maintaining product integrity, product package interaction, as well as maintaining the packages aesthetic.

- Plastics/PET/PP/HDPE/LDPE/PVC/PVDC/ Aclar
- Cold form foils
- Glass
- Metal/aluminum/steel
- Corrugate
- Paper
- Films
- Paperboard
- Adhesives
- Composites
- Multilayer
- Coatings











Hazardous (Potent) Compounds



CRB offers consulting services for the safety of patients and people from exposure, contamination and cross-contamination of hazardous compounds.

We have been providing designs to protect operators, products, facilities and health-care workers from highly hazardous and potent compounds for over 30 years. Our engineers are specialists with potent compounds and have unique backgrounds in process design, operations and process safety.

Consistent with current industry and International Society for Pharmaceutical Engineering (ISPE) trends, we use a risk-based approach to assess the containment needs for each process step. The risk-based approach is based upon the amount of the material present, the physical state and properties of the material, the unit operation being performed and the health hazard of the material. These considerations allow the owner to weigh the risks associated with each process step and make containment design decisions based on the relative hazard of that operation. This scientific approach provides a safe operation, and since containment decisions are made based on the physical needs of the process, it saves money at the end of the day.

Qualified Consultants to Assess Facilities:

- Have experience with current and developing technologies
- Participate in the ISPE Containment Community of Practice Steering Committee
- Utilize a risk-based approach that saves money and identifies risks
- Have experience with critical facility and process design

Applications for Containment of Hazardous and Highly Hazardous Compounds:

- Active pharmaceutical ingredients
- Sterile fill/finish
- Solid dosage
- Drug compounding
- Component weighing and sampling
- Analytical laboratories
- Research and development
- Quality testing

Design Considerations and Drivers:

- Facility layout: personnel, material, product and waste-flow issues
- Equipment design
- Room and equipment pressurization
- Gowning/degowning areas
- Storage of emergency gowning and breathing apparatus for facility recovery after an incident
- Decontamination and emergency response for equipment failure
- Personnel decontamination



Hazardous (Potent) Compounds





Experience with Containment Applications:

- Centrifuge discharging
- Container cleaning
- Reactor charging
- Tableting/encapsulating
- Sterile fill/finish
- Lyophilization
- Dispensary/weigh and break area
- Dryer charging and discharging
- Filter dryer discharging
- Final packaging/filling
- Laboratory-research and development
- Maintenance
- Material handling equipment
- Material movements and transfers
- Milling/sizing
- Warehouse shipping and receiving
- QC sampling-in-process
- Raw material sampling area
- Waste-stream handling



Oral Solid Dosage

No prepackaged solutions! At CRB, we understand that each manufacturer has unique needs, which is why we tailor our services to each client, ensuring that the solution you get is the best for you and not what was best for the last client. From greenfield designs and major renovations to troubleshooting a single piece of equipment, no issue is too big or too small. We pride ourselves in being our clients' long-term partner.

When designing an oral solid dosage manufacturing/packaging facility, it is important to incorporate a level of design that will fit both the needs and the budget of the project. We begin each design with our in-depth understanding of Current Good Manufacturing Practice (CGMP) and regulatory guidelines. We focus our goals around protecting the specific critical quality attributes of the product and streamline the process by identifying and controlling the critical process parameters. CRB follows this approach to ensure both the quality of your product and the efficiency of the process designed.

Fill Material

- Powder
- Liquid
- Bead
- Paste
- Tablet
- Mixed

Capsule Imprinting

- Axial
- Radial

Processing Influenced Attributes

- Particle Size
- Size Distribution
- Particle Shape
- Density
- Porosity
- Compressibility

Environmentally Influenced Attributes

- Hygroscopicity
- Light sensitivity
- Oxygen sensitivity

Safety

- Dust deflagration hazard
- Occupational exposure limits

Blending Techniques

- Direct compression
- Diffusive
- Convective

Tamper Proofing

Process

- Blenders (ribbon, cone, V, intermediate bulk containers, etc.)
- Weigh/dispense booths
- High-shear granulators
- Fluid bed processors
- Tablet presses
- Capsule fillers
- Coaters
- Printers
- Gel mixers/melters
- Gel transfer tanks
- Encapsulators
- Tumble/tray dryers
- Polishers
- Sorters
- Potent compound isolators
- Metal detectors
- Packaging equipment lines (bottle,





Oral Solid Dosage

fillers, blister and powder)

Design Expertise

- Dust collection/dust mitigation
- Explosion prevention
- Solvent recovery/abatement
- Dehumidification/humidification
- Filtration
- Room pressurization control
- Cross-contamination prevention
- Clean-in-place systems
- Vacuum
- Compressed air
- Reverse osmosis/deionized water
- Purified water
- Nitrogen
- Steam (clean/plant)
- Solvent containment
- Class 1/Division 1 and Class 2/Division 2 (dusts)
- Uninterruptible power supply
- Emergency power generation

Architectural Design

- Facility master planning
- Feasibility studies
- Environmental health and safety requirement incorporation
- Building code analysis and compliance
- Insurer compliance
- Lease compliance
- Risk analysis
- Material/people/waste flow
- Regulatory compliance
- Productivity maximization
- Cross-contamination minimization

- Light-sensitive product space design
- Staging (work in process) and circulation space planning
- Ergonomics
- Support space optimization
- Controlled substance environmental design
- Facility security
- Pest control
- Equipment delivery and access
- High hazard area design
- Passive fire protection design

Construction Management

- Site selection
- Program and project management
- Design management
- Estimating and budget development
- Scheduling
- Value engineering
- Construction logistics
- Life-cycle costing
- Constructability
- CGMP/qualification documentation
- Site supervision/utilization/logistics
- Safety management
- Quality control
- Scheduling
- Document control
- Subcontracting
- Equipment and material expediting
- Cost control and change control
- Cash flow projections
- Checkout and startup
- Construction support to validation









Regulatory Consulting



CRB has extensive experience working with the Food and Drug Administration (FDA) and other regulatory agencies in terms of setting industry guidance and designing and constructing facilities to meet Current Good Manufacturing Practice rules and regulations.

Pharmaceutical and Biotechnology Focused

With 80 percent of the firm's work in the pharmaceutical and biotechnology markets, we are focused and trained to design facilities that meet the strict regulations set forth by U.S. and international regulatory markets. Such projects require expert knowledge of the FDA regulations and guidelines and a thorough understanding of the challenges associated with critical operating environments. Several members of our staff come from operating companies and have direct knowledge and understanding of regulatory agency policies and procedures.

Industry Involvement

We have been heavily involved with the International Society for Pharmaceutical Engineering (ISPE) in developing and cowriting ISPE *Baseline® Guides* for the design and construction of pharmaceutical and biotechnology facilities, including "Sterile Manufacturing Facilities," "Water & Steam Systems," "Biopharmaceutical Manufacturing Facilities," "Packaging, Labelling, and Warehousing Facilities," "Bulk Pharmaceutical Chemicals," "Oral Solid Dosage," "Risk-Based Manufacture of Pharma Products" and "Biopharmaceutical Process Development and Manufacturing" with support and review on others. In many of these efforts, CRB employees were directly engaged with industry leaders and FDA staff to develop the documents. Involvement in other industry guidance documents include manyISPE *Good Practice Guides*, such as the "Ozone Sanitization of Pharmaceutical Mater Systems" and "Project Management for Pharmaceutical Industry."

Many of our people also maintain leadership positions in industry technical groups, including the American Society of Mechanical Engineers Bioprocessing Equipment and ISPE's Communities of Practice. We have also developed and participated in presentations with clients to the FDA, such as Type C meetings (requests for advice).

We strongly encourage our employees to attend seminars and training sessions in order to stay abreast of changing guidelines and industry trends, both within the United States and internationally.

Regulatory Authorities

CRB has designed facilities and projects for many international regulatory authorities:

- Food and Drug Administration
- Pharmaceutical Inspection Co-operation Scheme
- World Health Organization
- European Medicines Agency
- Health Canada
- China Food and Drug Administration
- Brazilian Health Regulatory Agency
- Central Drugs Standard Control Organization
- Pharmaceuticals and Medical Devices Agency
- Ministry of Food and Drug Safety
- Therapeutic Goods Administration

Validation

Along with validation staff members, we have an alliance with a large validation firm should additional resources be required. Services provided could include a validation master plan, internal training, field execution or operational qualifications.



Code Compliance Consulting

Does your facility comply?



It is your legal responsibility to conform to the constant changes and the standard of care for your building occupants. CRB offers consulting services to address the current building, fire and mechanical code requirements that impact your facility and its occupants.

Our in-house resources provide our domestic and international clients with specialized knowledge and expertise concerning regulatory requirements of hazardous materials, toxic gases, fire protection and building codes.

We have experience in providing evaluation, design and engineered solutions for the handling of all hazardous materials:

- Flammable gases and liquids
- Corrosive materials
- Potent materials
- Toxic and highly toxic substances
- Flammable and combustible materials
- Explosion mitigation for dusts, vapors and gases
- Secondary containment
- Off-site consequence analysis
- Material transport
- Materials of construction recommendations
- Alternate materials and methods



Code Compliance Consulting

Compliance by Design

CRB provides an authoritative source on construction and maintenance codes, National Fire Protection Association standards, American Society of Mechanical Engineers standards for compliance safety and to minimize liability. CRB regularly provides clients with customized presentations on applicable codes and standards tailored to building and process requirements.

Site Assessments

- Pre-construction evaluations
- Code compliance audits
- Environmental audits
- Chemical inventory analysis
- Review of required compliance documents
- Plans check review
- Management plan development

Advocacy Services

- Comprehensive code analysis
- Compliance assistance for all levels of government
- Alternate materials and methods

Educational Training

- Building, fire, mechanical and plumbing codes
- Plastic piping
- Process piping
- High purity piping
- Codes and materials of construction
- Hazardous materials
- Flammable and combustible material handling
- Toxic, highly toxic and reactive gases
- Potent compounds
- Legal requirements





Strategic Facility Planning

At CRB, we work closely with clients to provide them with the data and tools they need to manage their facility assets and align facility strategies with internal business planning requirements.

What is Strategic Facility Planning?

Our strategic facility planning team brings current and relevant space planning and utilization data and strategies to our clients. Whether you are planning for the short term (1-5 years) or embarking on long-term planning (6-20 years), having quality information allows you to understand the relationship between your business requirements and your facility requirements. The result is smarter, more cost-effective, facility decisions.

Our Strategic Facility Planning Methodology

Our strategic facility planning methodology typically includes an asset inventory or in-depth analysis of existing facility supply, a capacity analysis that identifies the extent of how the existing facilities can be used and a gap analysis that compares the facility supply to the business demands of the organization. When there is a gap between your facility supply and demand, our strategic facility planning team can work with you to develop scenarios for filling the gap. While this may include various growth scenarios, we can also assist you in exploring ways to increase your existing facility capacity through changes in space utilization, operation improvements and workflow efficiencies.

Who Needs Strategic Facility Planning?

Organizations that benefit from strategic facility planning services are those that are complex or changing in some manner. The nature of the change may be triggered by growth, reorganization, merger, centralization or updates to new technology. While strategic facility planning initiatives have traditionally been a focus of the private sector, the public sector is starting to follow suit. Tight funding and rigorous justifications for capital improvement have made both corporations and institutions think differently about space.

Strategic Facility Planning Data and Tools

Currently, strategic facility planning tools in the industry are many and varied. They typically include a combination of electronic floor plans and Excel spreadsheets or databases. Within an organization, strategic facility planning information is often piecemeal, unorganized and out of date. Our strategic facility planning team is on the forefront of innovation in data consolidation, management and reporting. We can help you streamline your data collection and analysis while leveraging your existing building databases as appropriate. Our team will help you identify the most cost-effective solutions to managing and analyzing your business planning data.





Strategic facility planning provides the data analytics our clients need to be more strategic with their master planning efforts.



Master Planning

CRB's approach for master planning is to provide leadership and a clear direction for the project in a friendly environment that facilitates open communication and brainstorming. With careful attention to the realities of budgets, schedules, regulatory requirements and engineering challenges, we support our clients in defining their goals and ultimately realizing their objectives.

Our planning team provides insight based on deep experience, and we channel that insight into appropriate strategies that form the basis for sound and feasible master plans that fit the varied needs of our technically driven clients. Every master plan is different, and CRB brings creativity to the planning process that yields unique ideas and solutions appropriate for the specific situation. Underlying this approach is our commitment to meeting client needs and our demonstrated skills in developing stakeholder support for master plans, which is critical to implementation.

Objective

Our objective is to prepare a master plan without compromising the functionality, convenience, appearance and longevity of an overall campus development. We develop comprehensive master plans to express our clients' history, mission, values and goals in a unifying image. Our planning documents provide in-depth information regarding several strategies and physical assets:

- Zoning and relationship to the community
- Open space
- Assessment of existing building infrastructure
- Identification of potential growth and expansion
- Functionality of building arrangements
- · Location of utilities, equipment and infrastructure support capabilities
- Vehicle and pedestrian circulation

Process

CRB utilizes an integrated planning approach using sustainability principles; we develop solutions that are operationally sound, fiscally responsible and environmentally feasible. We leverage new technology wherever possible and continuously identify opportunities for innovation. We seek to provide a financially viable plan that can be implemented following completion of the planning process. Our master planning staff members have diverse backgrounds, and we enlist the expertise of specialists within CRB to solve the most challenging problems.







Master Planning

One of the key differentiators of our Master Planning approach is our ability to assemble multidisciplinary, in-house teams led by experienced master planners who are capable of integrating the technical aspects of all disciplines into a comprehensive solution.

When our clients engage CRB to lead the preparation of their master plans, they have access to more than architectural planners; CRB specializes in Science and Technology facilities and facilitates a team-based approach that will result in a master plan that can be implemented throughout all disciplines:

- Research and Analysis
- Stakeholder Workshops
- Stakeholder interviews
- Planning & Design Charrette
- Alternative Scenarios & Preferred Concepts
- Draft Conceptual Plan
- Final Plan

Results

Our approach may differ from one project to another, but the objective is always the same: provide our clients with a financially feasible, demand-driven, and flexible roadmap for sustainable project development. Our master plans reflect our clients' vision of future Science and Technology facilities, while enhancing our clients credibility within the community. We appreciate the different "realities" and motivations associated with each project, and believe this appreciation leads to our success in implementing highly complex, technically driven projects.







Process and Packaging Simulation



There are a multitude of options to improve your facility, and process and packaging simulation will help you find the most cost-effective improvements. Whether it is an existing facility or a new design, process simulation will save you money.

The design of an efficient production plant is a complicated and time-consuming effort. It can be costly to do it properly and even more costly if done improperly. Process and packaging line simulation is a valuable tool to expedite the design process and save you money.

Process and packaging simulation is a computer representation of a unit operation, a single process train or an entire manufacturing plant. Because it is developed on a computer, you can quickly and easily study process alternatives before you risk capital expenditures. At CRB, we will work with you to construct an appropriate model, validate the model and conduct case studies. We provide training so you can use the model yourself to enhance throughput, reduce costs or study potential changes to your process.

We have no allegiance to any particular software package; we use the best commercially available tools for your application or develop custom tools if needed.

Chances are good that we have experience executing simulation projects for a process just like yours. Whether it is a quick capacity analysis, a debottlenecking study or a complete design for a new greenfield manufacturing plant, we will build an efficient model to find the answers you need. Process and equipment understanding is essential for developing an effective process or packaging model. Our extensive process design and operations experience is leveraged to get the right process data and the appropriate level of detail into your model, so you get the answers you need out of the model.



Process and Packaging Simulation

Process simulation adds value throughout the life cycle of the plant-from master planning through startup, debottlenecking and even day-to-day operations.

Master planning-lower capital cost and lower operating cost by creating a dynamic model that represents your manufacturing process

- Start with the business plan and manufacturing objectives
- Simulate each design scenario using your business plan as a guide
- Produce a lean design and enable lean operations
- Create faster and easier master plan updates as the market forecast changes

Facility design-evaluate process options to find the most economical plant design

- Risk reduction (risk of underperformance and over-design
- Improved designs (study many design alternatives in less time)
- Number and size of process and support Equipment
- Design data repository (keep all design parameters in one place: the model)
- Staffing requirements
- Production scheduling
- Utility capacity design
- Clean in place
- Waste handling system design
- Rightsizing of staging spaces

Debottlenecking-find the most costeffective method to get more product from an existing facility

- Maximum facility throughput
- Process and equipment bottlenecks
- Staffing and utility restrictions
- Scheduling constraints

- Reduction of work in process
- Effect of process variability and rework

Operations improvement—speed plant response time and reduce operating costs

- Use a process model in parallel with your plant
- Predict batch completion times
- Respond better to equipment failure and market demands
- Schedule production
- Improve communication
- Analyze sensitivity
- Improve layouts
- Improve compliance

Packaging

- Test what-if scenarios
- System performance projection
- Changeovers
- System challenge
- Accumulation
- Staging
- Efficiency improvements
- Warehousing operation
- Distribution strategies
- Capacity checks
- Work in process
- Truck and pedestrian traffic



Figure: Example of a Discrete Event Simulation Model buil



Operations Improvement (OI) Services

At CRB, we don't just design world-class manufacturing facilities; we also apply the latest operational improvement strategies to make them run more efficiently with less waste and lower costs.

In today's business environment, it is imperative that owners continually reduce operating expenses and demonstrate flexibility to make their sites viable locations for current manufacturing and the go-to sites for new products.

With Lean Six Sigma Master Black Belts and Green Belts on our team, CRB provides data-driven analysis to justify business decisions and prioritize projects to optimize manufacturing, warehousing and scientific environments. We have developed a unique approach and tool set to take a new look at your operations and cost structure to find significant cost-saving opportunities and develop specific, practical plans to act on them. Our approach addresses labor, core manufacturing, support processes and the facility itself. We start with a broad scope of all activities at your site and then quickly focus our efforts on the opportunities that will generate the highest return and require the least effort.

Our results translate to reduced cost and improved flexibility.





Operations Improvement (OI) Services

Approach

- Process understanding: We apply our analytical tools alongside your subject matter experts to map your process and identify the major cost contributors to your facility.
- Evaluation: We apply our process experience with our operations improvement tool set to develop a set of specific and actionable improvements.
- Develop a plan: With each recommendation, we will develop a detailed deployment plan and a forecasted, quantifiable return on investment.
- Presentation and buy-in: We communicate our findings and recommendations to key stakeholders striving to achieve commitment to the changes.
- Execution: We will continue to work with your staff to implement the recommendations, work through any remaining issues and meet all goals.

Tool Set

- Cost-of-goods analysis: Quantifies each cost contributor to highlight and prioritize the largest opportunities first
- Human capital optimization/value stream organizational design
- · Process simulation to optimize shared equipment, resources and labor
- Discrete event simulation: Current state versus projected changes
- · Layout optimization and facility of the future concepts
- Energy modeling: Analysis of energy use and costs
- · Risk assessment: Identify and quantify risks, improve system reliability
- Training: Empower people to maintain the improvements and continue to find new ways to streamline operations to further reduce costs
- Supply chain and cold chain: Optimize your entire supply network
- Business process modeling and statistical analysis

Expected Results

- Cost reduction: \$5-\$10 million/year for smaller sites, \$10-\$15 million/year for larger sites
- Up to 70 percent faster response to market demand
- Adaptable capacity to allow introduction of new products/processes
- Understand the impact of variability: Optimized inventory levels to handle demand variability
- Lean layouts: Right-sized facilities and reduced waste (non-value added activities)
- Fewer process deviations and retesting due to process stabilization
- Improved compliance
- Support for facility expansions and debottlenecking projects









Computational Fluid Dynamics Modeling

Whether CRB's clients are looking to improve the performance of an existing process or evaluate the feasibility of a new process, computational fluid dynamics (CFD) modeling can offer valuable insight to guide design decisions. Our CFD consulting practice allows designers and operators to visualize the flow of air or fluids in critical locations, even before a single wall is built.

We have a unique portfolio of CFD modeling experience for various high-tech applications. Our primary goal is to identify opportunities to optimize designs early in the process, allowing more informed decisions by all parties. Our CFD consulting practice focuses on scenario-based modeling:

- Clean-room air flow optimization
- Unidirectional air flow studies
- Data center energy optimization
- Mixing vessel modification

Case Studies | Proven Results

Data Center

We are focused on utilizing air-side economization to reduce the overall energy consumption associated with data center operation. The client's existing facility had issues due to excessive building pressure during full economization, and we wanted to prove that the design of the new building would mitigate these issues.

Due to the lack of research in the area of pressure drop through large building openings, we used CFD modeling to estimate the building pressure within the white space during full economization based on the actual building construction. The result was increased confidence that the new design could deliver the necessary performance without negatively impacting the functionality of the space.

Clean-room Air-flow Optimization

We were tasked with proving that unidirectional airflow could be achieved in two spaces during design.

The first space was a filling line with a restricted access barrier system, where we showed that the human machine interface was creating problems with the airflow patterns.

The second space, shown at the right, was a sterile storage tank room that required unidirectional airflow at six aseptic connections: three above the tanks and three near the bottom of the tanks. We observed a vortex that occurred around one of the aseptic connections and were able to adjust the air balance in the room prior to the commissioning phase to ensure proper airflow patterns.







