Mission Statement

ClinicalRM works to improve the quality of life in communities throughout the world by providing clinical research services with the highest standards of quality, integrity, and value.

Value Statement

As a company and as individuals, we pledge to develop loyal and satisfied customers by demonstrating a passion for our work and applying the highest standards of excellence to the services that we provide; to take on the most daunting challenges with a triumphant mindset; to value technology and change that lead to better efficiency, effectiveness, and corporate growth; to provide a positive work environment that facilitates continuous self-improvement; and to contribute positively to our community and environment.

PILOT BIOPRODUCTION FACILITY

Kimbra Cutlip, Writer

The Pilot Bioproduction Facility at WRAIR manufactures a variety of vaccines and biologics for Phase I clinical trials. The PBF is a multi-use facility and is compliant with federal regulations called Good Manufacturing Practices (GMP). Some of the vaccines manufactured at the PBF include those to prevent shigellosis, typhoid, cholera, dengue fever and Japanese encephalitis. Vaccine projects are focused on vaccine development for the Department of Defense, while additional clients come from private pharmaceutical and biotech companies as well as universities. The team works closely with clients and principal investigators to develop the production process and scale it up to clinical trial sized lots, all the while adhering to GMP regulations.

ClinicalRM has been staffing the PBF for over a dozen years, and while the production team has worked together throughout that time, some of them have been at PBF since its inception 20 years ago. That level of expertise and familiarity with each other has allowed them to handle some unique challenges and achieve notable success. "We've got a great track record for getting vaccines into Phase I," says PBF Chief Dr. Ken Eckels. "For example, the Japanese encephalitis vaccine that we produced and worked with from discovery all the way through licensure is the only FDA licensed JE vaccine in the U.S."

The vaccine production process: When a client provides the PBF with a culture of bacterial cells, Section Head Brian Bell and his team in Fermentation grow the source material into enough bacteria to create a vaccine. "It takes us about 24 hours to amplify a 1ml vial into about 20 kilos worth of cells," he says. He and his team continually monitor the conditions in a series of stainless steel vats (bioreactors) where they manipulate pH, temperature, growing medium, and a host of other parameters for optimal growth of the bacterial cells. It takes about a week to inoculate, grow and harvest vaccine antigens from the fermentation process.

That's when the Purification section takes over to extract the antigen that will be used to make the vaccine. "We use centrifugation, chemical extraction or column chromatography to purify between one and five grams of product," says Section Head, Jay Wood. Column chromatography involves passing the material through a gel that has a charge or a ligand (physical/chemical binder) that allows you to extract the required protein. Once purified, the protein is filtered and tested for release and stored.

The next step is formulation and fill. This is where Filling Section Head David Bradley steps in. In his Class 100 clean room, David mixes the final

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formulation before putting it into human dose vials and, when needed, freeze-dries the vaccine. "Dose wise, it depends on the vaccine," he says. "Our capacity for injectable vaccines is up to 2,000 vials."

While each of these steps can take between a few days and a couple of weeks to complete, additional time is required for preparation, documentation and interim phases where various aspects of the process are developed and refined.

Viral Vaccines

The process for creating viral vaccines is similar, with a few changes in the timeline, because the virus is inoculated into purified animal cells which take much longer to grow than bacterial cells. "It can take a number of weeks to amplify a 1 ml ampoule of cells into a liter or two of concentrated cells," says Russ Olson, Head of Viral Vaccines. After inoculating the cells with virus, it then takes seven to ten days to grow and harvest the virus. Purification for viral vaccines is similar to other vaccines in that contaminants are removed that may be harmful. Viral vaccine production can take anywhere from two to five weeks depending on the type of vaccine being produced.

The viral section is currently working on a vaccine for dengue fever. Throughout the process, the Viral Diagnostic Assay Development (VDAD) section tests the vaccine for purity and potency. Since dengue has four serotypes, four separate vaccines need to be manufactured then combined (formulated) into a tetravalent product. The VDAD lab also tests clinical specimens from subjects who receive the dengue vaccine. Viral neutralizing antibodies are measured; these antibodies indicate that they are protected from infection and disease caused by dengue. "The assay we developed here is the number one assay at the moment for DOD," says VDAD Section Head Rafael De La Barrera. "It's the only one that has been qualified for this use and is used for testing all our vaccines in clinical trials."

Transparency and Quality

Of course, as with every contract, achieving the goals while meeting all federal regulations is a top priority. That's the domain of Quality Assurance Manager Sandy Gibson and Quality Control Manager Mike Duran. "There are a lot of aspects to documenting and reviewing procedures and ensuring Good Management Practices," says Sandy. "You need to have a broad perspective and be involved with every aspect of it." She and Mike work closely together to maintain transparency and stay current on GMP. Mike, whose unit is responsible for releasing the final product says the focus is on purity, safety, identity, strength and quality. "We have to make sure the vaccines reach all the characterizations that they're supposed to," he says noting that the PBF now has a stability program that began a couple of years ago to assess the stability of a vaccine under different storage conditions.

Creating a vaccine for clinical trials is a complicated process that requires the integration of myriad discrete steps, all of which must work together. "We're brought all sorts of unique opportunities that follow general guidelines, but there's often an added twist, new clients to work with, new challenges to meet," says Deputy Chief Rick Millward. "We have an extremely talented team, and it's about getting everyone involved in sharing their expertise and knowledge to solve challenges together."

The team:

Ken Eckels, Chief, has been working at WRAIR for almost 30 years, having started in the Department of Hazardous Operations. With a PhD in microbiology, Ken has a scientific interest in dengue fever. He finds it particularly rewarding that GlaxoSmithKline is currently in Phase I trials with a vaccine made at the PBF. "When we make a vaccine that gets into Phase I and beyond it's tremendously rewarding--especially when you know that it's improving people's health and oftentimes, preventing death." Ken lives in Rockville, and has recently taken up golf as an alternative to the 10k races he used to run.

Rick Millward, Deputy Chief, has been at the PBF since 2001. As the Deputy Chief, Rick is now a government employee, but he spent his first five years with ClinicalRM as the QA Manager. He has a BS in biology. He says one of the most rewarding aspects of working at PBF is the diversity of projects and collaborating with his staff and clients to work through new challenges. "It's about the way we all interact. Because the PBF is relatively small, everyone's willing to wear different hats and share their knowledge in order to reach our goals. It's really about being part of a team." Fostering teamwork has been an important theme in Rick's career and home life. He's run bowling leagues and coached softball teams at previous places of employment and served as a volunteer coordinator for his daughter's youth orchestra. He's also won sev-

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eral awards during his 18-year-long involvement with Boy Scout leadership.

Susie Mathews, Administrative Coordinator, has been at PBF for 18 years. She began her career as a legal secretary and then went back to school for a B.S. in biology. She says the position is a good fit because it combines her office skills and secretarial skills with her biology degree. Susie handles all of the administrative work for the department, from the finances to equipment maintenance contracts to personnel training schedules and ID renewals. "I like working with people and I understand the manufacturing process and the vaccines. Things are always changing, which keeps me on my toes. We do good work and everybody's happy with what we do, so that's very rewarding." During her lunch break, Susie can often be found lifting weights at the gym on base—a passion she developed during her years as an amateur bodybuilder. At home, she and her toy poodle, BenGee, share their social time at a local hotspot for dogs and their owners.

Brian Bell, Head of Fermentation, has been with PBF for 21 years. He has a BS in biochemistry and chemistry. One of the things he enjoys most at the PBF is the sheer scope of responsibility and knowledge his job requires. "There are about eight different parameters running independently at all times, and every organism that grows inside that bioreactor has its own specific needs, so you have to know biochemically what they're doing and why are they doing it. Then you have to understand the mechanics of the fermentation technology to give them what they need." It's no surprise that Brian's an inveterate jack-of-all-trades at home, fixing everything himself and working on his own cars.

Jay Wood, Head of Purification, has been at PBF for 21 years. With an MS in biotechnology, he enjoys the creative challenges of his job. "I enjoy the variety and working with different customers from around the world, learning about their products and knowing that I'm part of the process of helping them along." The ingenuity and attention to detail he employs in his role as head of purification is reflected in his home life where he spends time rebuilding older BMWs. "Rebuilding an engine, you have to be detail-oriented. You learn as you go, because there's no one instructing you, so you have to use all the resources at your disposal." Jay also spends a lot of time on the softball diamond and traveling to national and international tournaments as an outfielder for a senior league team.

David Bradley, Head of Formulation and Fill, has been at the PBF for 19 years. Having spent his entire career in biotechnology, David has a long track record of scaling a process up from bench top to pilot scale. "It's rewarding when we get feedback from the client that the product is doing well in Phase I and looks promising for Phase II." Developing lyophilization (freeze drying) cycles and working with a new product on a weekly basis requires David's level of experience. The precision and attention to detail needed to work in a Class 100 clean room comes naturally to him and is reflected in his personal life, where he meticulously reloads some of his own ammunition before going to the shooting range.

Russ Olson, Head of Viral Vaccines, has been at the PBF for 14 years. Prior to that, he worked in biochemical engineering for ten years manufacturing HIV virus. Having worked with cell culture, virus isolation and virus production for most of his career, Russ says he's particularly interested in the biochemistry involved in his work. "There's a lot of chemistry involved in making the media for growing cells. It has to be very pure for growing cell culture, and each virus is a bit different, so you have to process it differently." Originally from Chicago, Russ has lived in Rockville, MD, for the past 30 years. When he's not reading or listening to classical music, Russ is likely to be found tinkering around the house.

Rafael De La Barrera, Head of Viral Diagnostics and Development, came to PBF in September of 2001. Growing up in a family with strong

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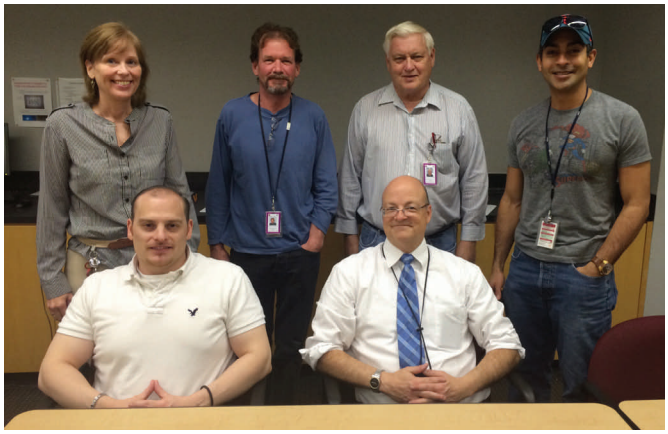
scientific interests, Rafael knew he wanted to work in a science field. He received an MS in biotechnology with a focus on molecular genetics. "I enjoy the immediate gratification of coming up with an idea and seeing it from beginning to end, determining whether or not it works and then presenting it to our partners and to Dr. Eckels, my boss." When he's not working, Rafael finds his gratification in far flung places and situations, from scuba diving in Australia to sky diving in Pennsylvania. He's currently planning trips to Italy and South Korea.

Sandy (second from left & family.)

Sandy Gibson, Quality Assurance Manager, has worked at the PBF for a little over a year and a half. She has a B.S. in medical technology and has worked in QA for the National Cancer Institute and handled GMP training, regulatory training and special QA projects for Science Applications International Corporation. QA is a good fit for Sandy because she enjoys the broad picture. "I like the holistic perspective. I'm exposed to the PIs, and to everything that goes into developing a product and putting it through clinical trials." Sandy says she's especially grateful to ClinicalRM for providing her with a flexible schedule, insurance assistance and a caring environment when she and her husband were struggling through his medical treatment for leukemia. Outside of work, Sandy fills her time renovating the 90-year-old home she and her husband own, and participating in home-building mission work in Appalachia.

Mike Duran, Quality Control Manager, has been with PBF since November of 2004. He has a B.S. in biology with a track in molecular biotechnology. He began his career at PBF in QA and then jumped over to fermentation to get a feel for the manufacturing aspect of the program. The move helped him recognize that his real interests lie in QC. "I wanted to work more in policy and interact more with clients, and QC touches on everything. Nothing's produced here that we're not involved with." The opportunity to explore his career interests has been important to Mike. "I've stayed with ClinicalRM specifically because they allowed me to get that experience and helped me do what I needed to grow." He has a predilection for list-making in all facets of his life, which has helped him to identify ways to improve a few processes at the PBF. During his free time, Mike plays piano and practices Taekwondo and the Korean sword art Gumdo.



Back Row—Sandy Gibson, Brian Bell, Russ Olson, Rafael De La Barrera

Front Row—Mike Duran, Rick Millward

ClinicalRM employees will be attending the following conferences in June.

Drug Information Association (DIA) Conference, June 15-19, San Diego Convention Center
http://www.diahome.org/en-US/Flagship Meetings/DIA2014.aspx

2014 BIO International Convention, June 23-26, San Diego Convention Center.
http: convention.bio.org/2014/

Scientists embark on unprecedented effort to connect millions of patient medical records. Read the entire article at:
http://wapo.st/1iWyUl5