

Rapid Progesterin-Based Endocrine Disruption Screening Assay

Fort Environmental Laboratories

515 South Duncan Street
Stillwater, OK 74074
Telephone: 405-624-6771
<http://www.fortlabs.com>

Environmental Problem

The endocrine system is a complex network of glands and hormones that regulates many of the body's functions, including growth, development, and maturation, as well as the way various organs operate. In recent years, concerns have been growing that certain chemicals in food, water, and other environmental media may be inadvertently disrupting the endocrine systems of humans and wildlife. A variety of endocrine-disrupting chemicals (EDCs) already has been discovered, and there is strong evidence that chemical exposure has been associated with adverse developmental and reproductive effects on fish and wildlife in particular locations. Many of these potential EDCs are present in the marketplace, where approximately 100,000-150,000 chemicals currently are available as medications, fertilizers, pesticides, and other products; approximately 2,500 new chemicals are released each year.

Passage of the Food Quality Protection Act in 1996 as well as amendments to the Safe Drinking Water Act reflect the concerns that some of these chemicals may pose significant risks to the endocrine systems of humans and animals. To address these concerns, EPA has developed a screening program to

determine whether certain substances have an endocrine effect. Conventional toxicology and product safety testing is expensive and time-consuming; with increasing concerns regarding the presence of EDCs in the environment, the need for rapid and efficient standardized assays and other screening tests has dramatically increased.

SBIR Technology Solution

With support from EPA's SBIR Program, Fort Environmental Laboratories (FEL) modified, developed, and standardized assays to test substances that might disturb reproductive and developmental processes in animals by interfering with the endocrine system. A modified *Xenopus laevis* oocyte maturation germinal vesicle breakdown (GVBD) model based on the work of Pickford and Morris (*Environ. Health Perspect.*, 107:285-292, 1999) for rapid evaluation of EDCs was developed as a possible Endocrine Disruptor Screening Program (EDSP) assay for EPA. An amphibian lifecycle (XLCA) model using *Xenopus tropicalis* to evaluate EDCs that affect the development of the reproductive tract also was developed and evaluated for commercialization.

The 24-hour GVBD assay was designed to evaluate environmental progestins and androgens *in vitro*. The chronic exposure model using *X. Tropicalis* was designed to specifically evaluate the impact of EDCs on sexual differentiation and reproductive fitness. The assays were standardized and evaluated by conducting a preliminary validation study with a series of known EDCs, compounds found to be inactive, and chemicals with unknown activity. By standardizing and validating these model sys-

tems for screening EDCs, FEL will provide the scientific community, chemical and pharmaceutical industries, appropriate regulatory agencies, and ultimately the public with a versatile short-term pre-screening assay. Further, this model will enhance understanding of the significance of the effects of EDCs on the reproductive systems of amphibians.

The technical feasibility of these models for screening potential EDCs is high. Although more work will be required to validate the models, it appears to fit the criteria established for emerging assays that currently are being sought for the EDSP.



Fort Environmental Laboratories developed models for rapid evaluation of endocrine-disrupting chemicals on reproduction and development.

Commercialization Information

FEL's assay is relatively straightforward and could be commercialized following method standardization and validation. The models are capable of broadly screening compounds with widespread endocrine activity, including estrogens, progestins, and androgens, which is desirable for EDSP tests. Because the tests are relatively inexpensive compared to many of the other proposed screening tests and many compounds can be tested simultaneously, these models are ideal.

The *in vitro* oocyte GVBD and amphibian lifecycle models will provide the scientific community with a cost-effective, rapid, and reliable method of testing EDCs. The ability to rapidly and cost-effectively screen for and evaluate the mechanisms of EDCs is an attractive alternative to the current laborious and expensive testing systems used today. Increasing concerns over the finding of EDCs in the environment have dramatically increased the need for standardized assays. FEL is well-positioned to capitalize on this emerging market as a pioneer and leader in this field.

Company History and Awards

Fort Environmental Laboratories, an environmental toxicology consulting firm and laboratory, is the only commercial laboratory in the United States to specialize in the toxicological study of amphibians and reptilian species. Co-founded in December 2000 by Drs. Douglas and Deanne Fort and



located in Stillwater, Oklahoma, FEL occupies a unique market niche because of the significant increase in interest in the use of these animals, as well as many others, as indicators of environmental health. FEL won the sole 2002 National Tibbett's

Award from the State of Oklahoma for "National Small Business Research Excellence" and was a finalist for the "Most Promising New Business" award from Oklahoma City's Oklahoma Venture Forum in 2002 and 2003.

SBIR Impact

- The widespread finding of endocrine-disrupting chemicals (EDCs) in the environment has dramatically increased the need for standardized assays.
- Fort Environmental Laboratories (FEL) developed model systems using *Xenopus* for rapid evaluation of EDCs.
- The models developed can broadly screen compounds with widespread endocrine activity and are ideal for high-throughput testing.
- FEL occupies a unique market niche because of the significant increase in interest in the use of these amphibians as indicators of environmental health.