Proposal Reviews

#192: Assessment of Hormonally Active Chemicals in the Central Valley Watershed: Monitoring, Activity Measurement, and Quantification of Adverse Effects.

University of California, Davis

Research and Restoration Technical Panel Review	
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Research and Restoration Technical Panel Review:

CALFED Bay-Delta 2002 ERP PSP
Research and Restoration Technical Panel Review Form

Proposal Number: 192

Applicant Organization: University of California, Davis

Proposal Title: Assessment of Hormonally Active Chemicals in the Central Valley Watershed: Monitoring, Activity Measurement, and Quantification of Adverse Effects.

Review:

Please provide an overall evaluation summary rating:

Superior: outstanding in all respects;
Above Average: Quality proposal, medium or high regional value, and no significant administrative concerns;
Adequate: No serious deficiencies, no significant regional impediments, and no significant administrative concerns;
Not Recommended: Serious deficiencies, significant regional impediments or significant administrative concerns.

Overall Evaluation Summary Rating	Provide a brief explanation of your summary rating
-Superior	**The proposed work is well justified based on the lack of information on endocrine-disrupting chemicals in the waters (freshwater) of the Bay-Delta and their potential impacts on fish populations and fish-eating populations in this area. The proposal is essentially a hunting expedition for hormonally active chemicals and the work load could become overwhelming and the study lose its focus at several points due to the massive number of water analyses proposed and the difficulty in prioritizing the laboratory exposures if numerous water samples displaying hormonal activity are found, and contain multiple hormonally active compounds. The panel recommends that a pilot study would be appropriate, especially if it focused on presumed worst case scenarios, to determine that a problem may indeed exist.**
-Above average	
-Adequate	
XNot recommended	

1. **Goals and Justification.** Does the proposal present a clear statement of goals, objectives and hypotheses? Does the proposal present a clear justification and conceptual model for the project?

   The goals are clearly stated, and based on the paucity of previously published findings of hormonally active compounds in agricultural drain water in the Central Valley and freshwaters of the Bay-Delta, the goal of better defining the extent and scope of this problem is timely and reasonable. However, this study was not deemed to be justified without more evidence that indeed ecologically relevant biological effects are an issuei.e. a pilot study is recommended.

2. **Likelihood of Success (Approach, Feasibility, Capabilities and Performance Measures).** Is the project likely to succeed based on the approach, feasibility and project team capabilities? Are the proposed performance measures adequate for measuring the project's success?

   Although the specific details for the particular tasks in the study (e.g. sampling sites for the study) are not provided in much detail, the strategy and approach described appear logical,and well thought out, and linked with one another. Success is highly dependent on initial phase of water sampling site selection (this process involving agricultural commissioners offices in 8 Central Valley counties is well described, and can be done with or without their cooperation) . Hormonal screening lab appears highly experienced and efficient in performing task 2, as is the CAHSF for task 3provided that the equipment requested in the budget is provided at ~$400K. If a long list of hormonally active compounds is identified in tasks 2 and 3, performance of all laboratory exposures and dosages necessary will be difficult and it is anticipated that this phase of the study could be a bottleneck.

   The reliance on in vitro bioassays exclusively is cause for concernmany false results are possible, and in vivo tests are strongly recommended to be included. The analytical complexity is daunting.

3. **Outcomes and Products.** Will the project advance the state of scientific knowledge in general and/or make an important contribution to the state of knowledge of the Bay-Delta Watershed? For restoration proposals, is the project likely to contribute to ecosystem restoration or species recoveries in a significant way? Will the project produce products useful to decision-makers and scientists?

   Valuable products and information could be provided by this study, and generation of negative results would be especially valuable, IF more relevant (e.g. in vivo) bioassays were used.

4. **Cost/Benefit Comments.** Is the budget reasonable and adequate for the work proposed?

   Overall, an expensive proposal, yet significant cost sharing was included in the proposal. A substantial amount, ~400K, for instrumentation, yet the workload would require dedicated instrumentation.

5. **Regional Review.** How did the regional panel(s) rank the proposal (High, Medium, Low)? Did the regional panel(s) identify significant benefits (regional priorities, linkages with other activities, local involvement) or impediments (local constraints, conflicts with other activities, lack of local involvement) to this proposal? What were they?

   Ranked medium to high by regional panels.

6. **Administrative Review.** Were there significant concerns about the proposal with regard to the prior performance, environmental compliance and budget administrative reviews? What were they?

   Some prior performance issues were raised, apparently relating to fiscal documentation disputes with the UC Davis, not with the PIs. Not clear how this would affect this proposal if funded. Environmental compliance and budget reviews did not show any problems.

Miscellaneous comments:

None

Delta Regional Review:

Proposal Number: 192

Proposal Title: Assessment of Hormonally Active Chemicals in the Central Valley Watershed: Monitoring, Activity Measurement, and Quantification of Adverse Effects.

Overall Ranking: **-**Low **X**Medium **-**High

Provide a brief summary explanation of the committee's ranking:

The proposal addresses an area that needs significant study. However, the proposed study does not address how it fits into a comprehensive plan. It also does not explain some choices for test species and sample locations. Tasks 2 and 3 would enhance other studies.

1. Is the project feasible based on local constraints?

   XYes **-**No

   How?

   No constraints. Simply a water quality study.

2. Does the project pursue the restoration priorities applicable to the region as outlined in the PSP?

   XYes **-**No

   How?

   Estrogen and like hormonally based compounds are a major concern. However this study does little to control them. It is simply a fact finding mission. It is a necessary first step, but should it be incorporated into a more comprehensive package.

3. Is the project adequately linked with other restoration activities in the region, such as ongoing implementation projects and regional planning efforts?

   -Yes **X**No

   How?

   This is an initial assessment and is not tied to anything else.

4. Does the project adequately involve local people and institutions?

   XYes **-**No

   How?

It involves a local university but no other local folks.

Other Comments:

Information on hormonally active compounds is a critical issue for the environment and drinking water.

The proponents dont specify why they propose to use gambusia instead of other toxicity test species like fat head minnows.

San Joaquin Regional Review:

Proposal Number: 192

Applicant Organization: University of California, Davis

Proposal Title: Assessment of Hormonally Active Chemicals in the Central Valley Watershed: Monitoring, Activity Measurement, and Quantification of Adverse Effects.

Overall Ranking: **-**Low **X**Medium **-**High

Provide a brief summary explanation of the committee's ranking:

This proposal uses experimental methods The proposal is to investigate a recently recognized, but not yet fully characterized, potentially wide-spread aquatic contaminant. The subject is important, but the investigation is very wide-ranging; the sampling effort may overwhelm the analytical capability; and the choice of test organism, mosquito fish, is an introduced, environmentally tolerant species.

1. Is the project feasible based on local constraints?

   -Yes **X**No

   How?

   The proposal is ambitious, proposing a huge sampling program, but has not yet determined the sites. The large group of contaminants do not have established methods. There are so many unknowns in the investigation, it is hard to imagine that all the tasks can be completed within the timeframe of the grant.

2. Does the project pursue the restoration priorities applicable to the region as outlined in the PSP?

   XYes **-**No

   How?

   The proposal targets toxicity of unknown origin, a problem thought to extend throughout the Bay/Delta area.

3. Is the project adequately linked with other restoration activities in the region, such as ongoing implementation projects and regional planning efforts?

   XYes **-**No

   How?

   The proposal states that sampling is to be coordinated with other research efforts and that the investigators will work with a group that is developing analytical methods for these compounds.

4. Does the project adequately involve local people and institutions?

-Yes **X**No

How?

There is no evidence in the proposal of interaction with local people or institutions.

Other Comments:

The proposal addresses an important question, but at this stage, the number of variables the investigation must work with make the outcome uncertain. A less ambitious, better focused project might be more appropriate.

Sacramento Regional Review:

Proposal Number: 192

Applicant Organization: University of California, Davis

Proposal Title: Assessment of Hormonally Active Chemicals in the Central Valley Watershed: Monitoring, Activity Measurement, and Quantification of Adverse Effects.

Overall Ranking: **-**Low **-**Medium **X**High

Provide a brief summary explanation of the committee's ranking:

EDC's have been shown to be potenially important factors that may be adversely affecting aquatic biota. Subsequent review panels should compare this proposal with other similar EDC study proposals (such as #6) and determine their relative merits.

1. Is the project feasible based on local constraints?

   XYes **-**No

   How?

   Project uses standard, accepted protocols for monitoring/assessment of EDC's.

2. Does the project pursue the restoration priorities applicable to the region as outlined in the PSP?

   XYes **-**No

   How?

   The proposal to address ecosystem impacts from EDC's addresses issues raised in PSP Sac Region Restoration Priority #7.

3. Is the project adequately linked with other restoration activities in the region, such as ongoing implementation projects and regional planning efforts?

   XYes **-**No

   How?

   This relates to the general concern of EDC's in the Bay/Delta, however there is no specific planning or implementation program to link to. Should be reviewed to determine link to the SRWP's Strategy to Address Toxicity of Unknown Causes.

4. Does the project adequately involve local people and institutions?

   XYes **-**No

How?

This type of research and assessment does not require significant involvement of locals or other institutions, however, involvement of locals and coordination with related activities (e.g. SRWP and Sacramento River Conservation Area activities) seems to be generally missing from this proposal.

Other Comments:

1. If funded, this project should provide for some level of communication with affected local constituencies and with other related studies (e.g. regular reporting to Sacramento River Conservation Area Board and coordination with the SRWP Toxics Committee).

External Scientific: #1

Research and Restoration External Scientific Review Form

Proposal Number: **192**

Applicant Organization: **University of California, Davis**

Proposal Title: **Assessment of Hormonally Active Chemicals in the Central Valley Watershed: Monitoring, Activity Measurement, and Quantification of Adverse Effects.**

Conflict of Interest Statements:
I have no financial interest in this proposal.
XCorrect
-Incorrect

In the blank below please explain any connection to proposal, to applicant, co-applicant or subcontractor or to submitting institution (write "none" if no connection):

None. I have worked with Fry in the past (8 years ago) on another project. I am associated with Johnson and Werner through the unrelated Campuswide Ecotoxicology Program. I am aware of the work of Dennison, but do not know him personally. We are all housed in different departments on the UC Davis campus.

Review:

Please provide an overall evaluation summary rating:

Excellent: outstanding in all respects;
Good: quality but some deficiencies;
Poor: serious deficiencies.

Overall Evaluation Summary Rating	**Provide a brief explanation of your summary rating**
XExcellent	**See general comments above. As I said, this is an excellent proposal that is well-done technically, well-planned, and highly applicable to stated CALFED goals on contamination evaluation; highly achievable and potentially leading to further more specific studies that will define specific problems and problem areas. This will benefit restoration planning.**
-Good	
-Poor	

1. **Goals.** Are the goals, objectives and hypotheses clearly stated and internally consistent? Is the concept timely and important?

   The goals are as outlined by CALFED, and very specific to the objectives listed. This project essentially proposes to monitor water for a myriad of potentially hormonally-active materials (EDs) in the CALFED area of interest, to map them and relate them to use-patterns (if known), to evaluate their risks to fish through bioassay work on a common species (exotic) in the system and with biochemical techniques, to project risks to other species in the system, and to conduct outreach on the work. All these goals are specifically

stated and follow from one-another. It is a fairly standard approach used in ecological risk-assessment, so techniques are well established. Another goal is to further develop some promising bioassay techniques. When I read the proposal, I was struck in that I more-or-less viewed it as basically a "Lake-Michigan type project", with very specific goals on endocrine disrupters (and where much pioneering work has been done on EDs). Needless to say, I have great regard for the "Lake Michigan approach", and that project has been highly productive and successful. I was pleased to see that the proposal has a stated outreach objective, as well, something unusual from what I have seen.

A few of the hypotheses are a bit nebulous but specifically stated in most cases. Interestingly, hypothesis 1A, for example, is more of a statement of approach than a testable hypothesis. Interestingly if Ho of Hypothesis 1 is accepted, then no more work would be needed; but it fairly presents the problem, and it is highly unlikely that some important EDs would be found in this project. But one potential weakness or omission I perceived, perhaps just not adequately stated, was that the goals do not seem to address the potential for quantitating seasonal variability (a testable hypothesis) in ED inputs. An unstated benefit that I perceived from this proposal was that this project will be taking the approach of looking at most POPs in the search for EDs; and the total data-base, regardless of EDs, will have the added benefit of summarizing or evaluating many additional compounds in the CALFED area of interest that comply to larger contamination evaluation objectives (i.e., there is more there than stated). In total, the goals of the project follow logically through a sensible and established pattern in ecotoxicological studies to achieve various risk-assessment goals needed by CALFED.

Hopefully, the project will lead to specific studies in specific problem areas as the evaluations come in. Overall, the stated goals are reasonable and acheivable. I think this is the correct approach; and the biggest challenge will be to keep leadership and coordination among the team members consistent and coordinated throughout the duration of the proposed project.

2. **Justification.** Is the study justified relative to existing knowledge? Is a conceptual model clearly stated in the proposal and does it explain the underlying basis for the proposed work? Is the selection of research, pilot or demonstration project, or a full-scale implementation project justified?

   From all that has been coming-out in the literature in the past 5-10 years, there are many unknown potential ecotoxicological problems associated with "old" and "new" (or even just newly-discovered) environmental contaminants, so that this study is very timely. The research team is ahead already in that they have conducted a pilot study that seems to indicate there are potential problems with EDs that are to be expected. The existing knowledge of EDs has primed this kind of work for the CALFED area of interest.

3. **Approach.** Is the approach well designed and appropriate for meeting the objectives of the project? Are results likely to add to the base of knowledge? Is the project likely to generate novel information, methodology or approaches? Will the information ultimately be useful to decision-makers?

   I have already made comments on the approach and as I said above, I think this is the right approach for the questions at this stage of our knowledge about EDs in the specific area of interest. I think the project is especially fortunate, if approved to have some of the best leading-edge research on bioassay and biomarkers being applied to a likely problem in the CALFED area of interest. The approach of chemical identification of active chemicals that have been indentified as such illustrates the logical and systematic approach (not the "shotgun approach") that will be taken in this project. The idea of mapping contaminant loads in relation to use-figures when available is especially useful in the outreach portion of the study (I hope they

will make it all available on a web-site). I also commend the authors for selecting the mosquitofish as a bioassay species (as clean, lab-reared individuals), because it is also commonly found throughout the ecosystems they propose to sample, and this will allow more meaningful comparisons eventually between laboratory tests and field samples.

I believe the approach does exactly what is needed for the questions being asked, and the approach is correct for the CALFED goals ; they have made a good selection of their indicator species (common, easy to collect, responsive, and probably will not die from the bioassay work and/or chemical exposures). The study appears to be well-planned.

4. **Feasibility.** Is the approach fully documented and technically feasible? What is the likelihood of success? Is the scale of the project consistent with the objectives?

   See above comments. There is a high liklihood of success because the approach builds from one step to the other. The large scale of the project will make-for some logistical difficulties but these are easily achievable with adequate time in the field and careful sampling, and timing of samples. This is an impressive proposal that is well-planned and well-written. I actually enjoyed reading through it!

5. **Project-Specific Performance Measures.** Does the project include appropriate performance measures to measure success relative to the project's goals and objectives? Is there enough detail as to how the performance measures will be quantified? For restoration projects, are monitoring plans explicit and detailed enough to determine if performance measures will be adequately assessed?

   Because of the strong statements by CALFED RFP planners (outlined on this proposal as outlined under "the applicability to CalFed ERP and Science Program goals", I am surprised that more proposals on EDs did not appear; but this proposal is as close as any I have reviewed to meeting CALFED goals, and with specific performance measures. The performance measures as stated in the proposal are not overly stated nor do they imply that results and products will not be met. Hopefully, results will lead to more specific studies on more specific compounds of interest in the region.

6. **Products.** Are products of value likely from the project? Specifically for restoration projects, are products of value also likely from the monitoring component? Are interpretative outcomes likely from the project?

   This is hard to judge except for the scientific products of the project, which are likely to be extensive and useful. As I said above, it was encouraging to see that an outreach component of the project is actually stated as a goal and that represents a desirable product as well; and that will help insure that the results of these studies will readily and rapidly move from researcher to manager; and will also form a strong basis for adequately planning furure studies of a more specific nature at potential "hot spots" in the CALFED area of interest.

7. **Capabilities.** What is the track record of applicants in terms of past projects? Is the project team qualified to efficiently and effectively implement the proposed project? Do they have available the infrastructure and other aspects of support necessary to accomplish the project?

   The team of investigators on the proposal represent expertise in endocrinology and, specifically, EDs; fish ecotoxicology and aquatic toxicology investigators working in a laboratory on the UCD campus with an international reputation in aquatic toxicology (with much previous expertise in evaluating ecological effects of various compounds on fish physiology and fish populations); an expert on risk assessment and ecotoxicology (being also an excellent ecologist);

and a recognized biochemist and ecotoxicologist working on unique and innovative biomarkers, which are bound to improve with experience as this study progresses.

8. **Cost/Benefit Comments.** Is the budget reasonable and adequate for the work proposed?

   The budget for this study is reasonable in light of the equipment and expertise that will be needed to develop the endpoints. In fact, the budget is almost minimal in relation to what is proposed as being accomplished. I estimate that about 1/3 will be spent for sophisticated, but very current equipment needed for the sophisticated and difficult analytical chemistry required. I view this actually as an investment by CALFED whereby future studies can be carried-out that utilize state-of-the-art technology, and thus yield the best, most updated results.

Miscellaneous comments:

I found this to be a well-written and well-conceived project that refreshingly addresses some of the specific questions about EDs that have been raised for the CALFED area of interest as well as many other areas, worldwide.

External Scientific: #2

Research and Restoration External Scientific Review Form

Proposal Number: **192**

Applicant Organization: **University of California, Davis**

Proposal Title: **Assessment of Hormonally Active Chemicals in the Central Valley Watershed: Monitoring, Activity Measurement, and Quantification of Adverse Effects.**

Conflict of Interest Statements:
I have no financial interest in this proposal.
XCorrect
-Incorrect

In the blank below please explain any connection to proposal, to applicant, co-applicant or subcontractor or to submitting institution (write "none" if no connection):

None

Review:

Please provide an overall evaluation summary rating:

<u>Excellent:</u> outstanding in all respects;
<u>Good:</u> quality but some deficiencies;
<u>Poor:</u> serious deficiencies.

Overall Evaluation Summary Rating	**Provide a brief explanation of your summary rating**
XExcellent	**The proposed work is highly justified based on the lack of information on endocrine-disrupting chemicals in the waters (freshwater) of the Bay-Delta and their potential impacts on fish populations and fish-eating populations in this area. The proposal is well-conceived at all points, and follows a logical approach to addressing its goals. However, it is essentially a hunting expedition for hormonally active chemicals and the work load could become overwhelming and the study lose its focus at several points due to the massive number of water analyses proposed and the difficulty in prioritizing the laboratory exposures if numerous water samples displaying hormonal activity are found, and contain multiple hormonally active compounds. The proposal would be improved by providing more detail in terms of sampling site location and methods of analysis and experimentation, and from the numerous typographical errors appears to have been put together very quickly. However, because of the ecological importance of this issue to both California and the nation as a whole, the relative lack of information in the watershed to be studied, its justification based on CALFED objectives, the well-conceived and logical approach described in the proposal, and the past track record of the applicants, my overall rating for this proposal is good to excellent.**
-Good	
-Poor	

1. **Goals.** Are the goals, objectives and hypotheses clearly stated and internally consistent? Is the concept timely and important?

   Based on the paucity of previously published findings of hormonally active compounds in agricultural drain water in the Central Valley and freshwaters of the Bay-Delta, the goal of better defining the extent and scope of this problem is timely and reasonable. The goals are clearly stated.

   Rating--excellent

2. **Justification.** Is the study justified relative to existing knowledge? Is a conceptual model clearly stated in the proposal and does it explain the underlying basis for the proposed work? Is the selection of research, pilot or demonstration project, or a full-scale implementation project justified?

   Such a study is justified because of preliminary data documenting hormonally active compounds in agricultural drain water in the Central Valley, and the general lack of good data on levels and geographic distribution of these chemicals in the Central Valley. Because of the potentially significant impact of endocrine disrupting chemicals on fish, wildlife and human populations, the goals of this study are very important. The choice to screen water samples based on hormonal activity seems logical and cost-effective, takes into account the possible synergistic effects of multiple hormally active chemicals likely to be encountered, and is a logical way to estimate environmental risk rather than going on a "hunting expedition" by the expensive path of simply measuring hundreds of chemicals in over 1000 water samples. Moreover, such an approach will likely identify chemicals with previously unknown hormone activity.

   Rating--very good

3. **Approach.** Is the approach well designed and appropriate for meeting the objectives of the project? Are results likely to add to the base of knowledge? Is the project likely to generate novel information, methodology or approaches? Will the information ultimately be useful to decision-makers?

   All tasks described in the the approach are relatively straightforward, and are developed in a very logical sequence with respect to addressing the study objectives. The approach involves 1) initial collection of massive numbers of water samples (by filtration through solid phase extraction cartridges/disks) from agricultural drains, municipal water treatment outfalls, etc., throughout the multicounty sampling area followed by 2) hormonal activity screening by proven methods to measure estrogenic and androgenic activity using recombinant cell lines transfected with estrogen or androgen-responsive luciferase reporter genes (with logical and well-described positive and negative controls), 3) analytical identification of hormonally active compounds from samples with positive activity in the hormonal screens above (to be done by an experienced, high-volume analytical lab Calif. Animal Health and Food Safety Lab-CAHSF), 4) laboratory screening of hormonally active compounds by lab exposures using the mosquito fish (a good species of choice considering its broad distribution in the watersheds to be sampled in this study, and its performance in previous laboratory culture and exposures), using endpoints such as #s of live young, sex ratios of progeny, fertility, histopathological conditions, and appropriate biomarkers such as vitellogenin and choriogenin (previously developed and used in medaka by researchers participating in this study) as markers of reproductive function, followed by 5)data evaluation, outreach and project management (adaptive management of water sampling

design and focus on problem areas discovered in tasks 1-4). A significant feature of this last task is the ability to correlate the data from water samples and hormonal screens with maps of specific pesticide, herbicide, and associated chemical (e.g. alkylphenols) usage in unique geographical areas that are avai lable from Calif DPR. From these data correlations, further water sampling strategies can be developed.

Although the specific details for the particular tasks in the study (e.g. sampling sites for the study) are not provided in much detail, the strategy and approach described appear logical,and well thought out, and linked with one another.

Rating--excellent

4. **Feasibility.** Is the approach fully documented and technically feasible? What is the likelihood of success? Is the scale of the project consistent with the objectives?

   Success is highly dependent on initial phase of water sampling site selection (this process involving agricultural commissioners offices in 8 Central Valley counties is well described, and can be done with or without their cooperation) . Hormonal screening lab appears highly experienced and efficient in performing task 2, as is the CAHSF for task 3provided that the equipment requested in the budget is provided at ~$400K. The Animal Toxicology Laboratory and its personnel at UC Davis have extensive experience in small fish husbandry and performing the laboratory exposures described, and year one is provided for setting up the laboratory exposure facility and methods. If a long list of hormonally active compounds is identified in tasks 2 and 3, performance of all laboratory exposures and dosages necessary will be difficult and it is anticipated that this phase of the study will be the main bottleneck. However, this drawback is directly addressed in the proposal as is the strategy for prioritization of testing of compounds in this phase.

   Rating--very good

5. **Project-Specific Performance Measures.** Does the project include appropriate performance measures to measure success relative to the project's goals and objectives? Is there enough detail as to how the performance measures will be quantified? For restoration projects, are monitoring plans explicit and detailed enough to determine if performance measures will be adequately assessed?

   The numerous decision points occurring at the various phases of the study and the consultations involved, the past good track record of the applicants, and the quarterly reporting of results should ensure success of this project, although the reviewer is somewhat skeptical that the planned collection and analysis of well over 1000 water samples/year can be accomplished. Also, if the screening phase of the study identifies numerous samples with multiple hormonally active compounds, the testing of synergistic effects in the laboratory exposure phase may become difficult if not overwhelming.

   Rating --good

6. **Products.** Are products of value likely from the project? Specifically for restoration projects, are products of value also likely from the monitoring component? Are interpretative outcomes likely from the project?

   Valuable products and information should be provided by this study, especially the important "negative" information on lack of hormonal activity from the the bulk of the samples that is likely from this study. A strong point of the study is its ability to document synergistic effects of multiple hormonally active compounds in the laboratory exposure phase, assisting

regulatory agencies in formulating pesticide and herbicide use regulations in situations where single compound levels may not exceed the maximum permissible exposure levels.

Rating--very good

7. **Capabilities.** What is the track record of applicants in terms of past projects? Is the project team qualified to efficiently and effectively implement the proposed project? Do they have available the infrastructure and other aspects of support necessary to accomplish the project?

   The track record of all applicants in the proposal is quite good, and the UC Davis infrastructure and level of cooperation among the various labs is quite strong and experienced in studies such as this.

   Rating--excellent

8. **Cost/Benefit Comments.** Is the budget reasonable and adequate for the work proposed?

   Based on current continuous usage of analytical chemistry instruments and need to purchase new equipment and replace aging instruments, request of 403K for additional equipment to augment current instruments seems necessary, but is a major portion of budget. However, the high volume of samples to be chemically analyzed in this proposal seems to require these purchases. A strong point in the budget is the fact that among the several applicants a significant proportion of their time on this proposal will not be charged; in fact, only Fry will be charging salary (from what I can tell, 2/3 of his salary and benefits) for project oversight, water sampling strategy decisions, and program management. The remaining applicants listed will not be charging salary in the budget. Unfortunately, the budget justification section has numerous typographical errors in it, making interpretation of the specific budget items somewhat difficult at times.

   Rating--very good

Miscellaneous comments:

External Scientific: #3

Research and Restoration External Scientific Review Form

Proposal Number: **192**

Applicant Organization: **University of California, Davis**

Proposal Title: **Assessment of Hormonally Active Chemicals in the Central Valley Watershed: Monitoring, Activity Measurement, and Quantification of Adverse Effects.**

Conflict of Interest Statements:
I have no financial interest in this proposal.
XCorrect
-Incorrect

In the blank below please explain any connection to proposal, to applicant, co-applicant or subcontractor or to submitting institution (write "none" if no connection):

None

Review:

Please provide an overall evaluation summary rating:

Excellent: outstanding in all respects;
Good: quality but some deficiencies;
Poor: serious deficiencies.

Overall Evaluation Summary Rating	**Provide a brief explanation of your summary rating**
-Excellent	**Though potentially of great concern in terms of human health and wildlife populations, there is apparently so little information on the existence or impacts of endocrine disrupting chemicals in the CalFed region that it would seem a scaled down pilot study, aiming for likely worst-case exposures, would be a more effective approach to determining whether these chemicals are priority risk agents in the region. A more detailed in-depth study could be commenced on the basis of results of the pilot study if necessary.**
XGood	
-Poor	

1. **Goals.** Are the goals, objectives and hypotheses clearly stated and internally consistent? Is the concept timely and important?

   The objectives of the project are: 1) to provide a detailed assessment of chemicals present in the Sacramento-San Joaquin watersheds with have reproductive hormonal activity; 2) to identify and quantify these chemicals; 3) to determine adverse effects of individual chemicals on mosquito fish (Gambusia affinis), and 4) perform an environmental hazard assessment of these chemicals.

Concern with the effects of hormonally active chemicals on humans and wildlife is a very timely topic of research. The hypotheses to be tested in this project are clearly stated.

2. **Justification.** Is the study justified relative to existing knowledge? Is a conceptual model clearly stated in the proposal and does it explain the underlying basis for the proposed work? Is the selection of research, pilot or demonstration project, or a full-scale implementation project justified?

   The applicants simply state that hormonally active chemicals are present in the Central Valley watershed and refer to Johnson et al. 1998. This is really all of the justification provided with the exception of brief of other areas (e.g., U.K.) effects of endocrine disruptors in fish have been identified. However, this is not to say that endocrine disruptors are not a potentially important problem - it is just that very little information exists particularly with regard to their population level consequences. However, it could be considered that the present project be reduced to a small pilot study that would be used to identify likely worst-case environmental concentrations prior to conducting a full-scale study.

3. **Approach.** Is the approach well designed and appropriate for meeting the objectives of the project? Are results likely to add to the base of knowledge? Is the project likely to generate novel information, methodology or approaches? Will the information ultimately be useful to decision-makers?

   Sources of uncertainty in the present approach include 1) to what extent Gambusia affinis is an appropriate model for detecting endocrine disruption in fish and 2) the extent to which alterations in endocrine function are linked to ecologically relevant effects on fish population dynamics. Gambusia does have the advantage that it is widespread in the study area. It would be useful to know how it compares in sensitivity to endocrine disruptors relative to other commonly tested species (e.g., Japanese Medaka). It appears that this question will be addressed during year 1 of the study.

   For human health risk assessment in which the target is the individual, demonstrating of changes in biochemical or physiological performance (such as endocrine activity) may be considered an appropriate endpoint. However, for fish species (where the target of protection in generally the population) there is serious debate as to how to interpret changes in endocrine activity per se in assessing risks to populations.

   An advantage of the approach is that intact water samples will be analyzed for hormonal activity. As the applicants point out, exposure is likely to be to combinations of chemicals and the possible adverse effects are based on the sum total of hormonal activity in the water sample as a whole.

   The method for detecting estrogenic and androgenic activity is an in vitro technique employing human cell lines. Although these methods may be advantageous for screening large numbers of samples there have been concerns (both with regard to false positives and false negatives) as to the reliability of in vitro methods compared to in vivo and my impression is that the latter are generally preferred.

   Also, it is stated that the chemicals identified will be compared to analytical standards. What about possible metabolites and/or breakdown products of chemicals - which may have hormonal activity but for which standards are unlikely to exist?

4. **Feasibility.** Is the approach fully documented and technically feasible? What is the likelihood of success? Is the scale of the project consistent with the objectives?

   Whether it is possible to single out individual chemicals from a complex mixture for testing will be dependent on the complexity of the mixture. For example, water samples dominated by a few chemicals in relatively high concentrations will be easier to deal with (in terms of identification and subsequent single-chemical testing) then samples consisting of a large number of chemicals in small concentrations. Since sampling will be focused on areas where very complex mixtures may be expected to occur (e.g., municipal outfalls), this could prove analytically challenging.

   It is stated that the selection of chemicals for fish evaluation will be based on consideration of the amount of each possible chemical applied or used in the watershed - is this information readily available (other than for pesticides) and if so from whom?

5. **Project-Specific Performance Measures.** Does the project include appropriate performance measures to measure success relative to the project's goals and objectives? Is there enough detail as to how the performance measures will be quantified? For restoration projects, are monitoring plans explicit and detailed enough to determine if performance measures will be adequately assessed?

   Performance measures will largely revolve around ensuring that the analytical extraction and analysis methods are sufficiently accurate, precise and reproducible. There are straightforward and quantitative methods for doing this.

6. **Products.** Are products of value likely from the project? Specifically for restoration projects, are products of value also likely from the monitoring component? Are interpretative outcomes likely from the project?

   The primary products expected from the project are peer-review articles and meeting presentations. High concentrations of particular chemicals or samples that cause reproductive impairments in Gambusia will be reported to the appropriate authorities.

7. **Capabilities.** What is the track record of applicants in terms of past projects? Is the project team qualified to efficiently and effectively implement the proposed project? Do they have available the infrastructure and other aspects of support necessary to accomplish the project?

   The project team had strong qualifications and has the appropriate expertise to carry out this project. In terms of infrastructure and support, the applicants are applying for additional analytical equipment that is necessary to conduct the proposed project.

8. **Cost/Benefit Comments.** Is the budget reasonable and adequate for the work proposed?

   This project is for 3 years and has a total budget of 1,838,343. It appears that many of the labor hours will be covered by the university at no cost to the project. Expenses appear reasonable with respect to the kinds of analyses to be performed.

Miscellaneous comments:

None

Prior Performance/Next Phase Funding:

New Proposal Number: 192

New Proposal Title: Assessment of Hormonally Active Chemicals in the Central Valley Watershed: Monitoring, Activity Measurement, and Quantification of Adverse Effects.

1. Prior CALFED project numbers, titles, and programs: (*list only projects for which you are the contract manager*)

   ERP 99-N07 ? Chronic Toxicity of Environmental Contaminants in Sacramento Splittail- A Biomarker Approach

2. Prior CVPIA project numbers, titles, and programs: (*list only projects for which you are the contract manager*)

   N/A

3. Have negotiations about contracts or contact amendments with this applicant proceeded smoothly, without persistent difficulties related to standard contract terms and conditions?

   -Yes **X**No **-**N/A

   If no, please explain any difficulties:

   The Office of Vice Chancellor for Research at UC Davis has requested numerous and repeated requests for revisions of the standard contract terms. Only a few of these issues were raised in the PSP process. Reconciling these issues has required extensive staff time for CALFED and other State agencies. This repeated negotiation has resulted in a delay of contract execution for up to 2 years.

4. Are the status, progress, and accomplishments of the applicant's current CALFED or CVPIA project(s) accurately stated?

   XYes **-**No **-**N/A

   If no, please explain any inaccuracies:

5. Is the applicant's progress towards these project(s)' milestones and outcomes to date satisfactory?

   XYes **-**No **-**N/A

   If no, please explain deficiencies:

6. Is the applicant's reporting, records keeping, and financial management of these projects satisfactory?

   XYes **-**No **-**N/A

If no, please explain deficiencies:

UC Davis has had consistent difficulty communicating internally and externally regarding its fiscal documentation. Reconciling financial issues with UC Davis has proved very problematic. The financial situations raised by UC Davis have proved to be the most difficult within the NFWF managed CALFED contracts.

7. Will the project(s) be ready for next phase funding in 2002, based on its current progress and expenditure rates?

XYes **-**No **-**N/A

If no, please explain:

Other Comments:

The difficulties expressed above are limited to UC Davis campus only.

The Principal Investigators and other project researches have been very professional and effective in meeting the goals of the project.

Environmental Compliance:

Proposal Number: 192

Applicant Organization: University of California, Davis

Proposal Title: Assessment of Hormonally Active Chemicals in the Central Valley Watershed: Monitoring, Activity Measurement, and Quantification of Adverse Effects.

1. Are the legal or regulatory issues that affect the proposal identified adequately in the proposal?

   XYes **-**No

   If no, please explain:

2. Does the project's timeline and budget reflect adequate planning to address legal and regulatory issues that affect the proposal?

   XYes **-**No

   If no, please explain:

3. Do the legal and regulatory issues that affect the proposal significantly impair the project's feasibility?

   -Yes **X**No

   If yes, please explain:

Other Comments:

Budget:

Proposal Number: 192

Applicant Organization: University of California, Davis

Proposal Title: Assessment of Hormonally Active Chemicals in the Central Valley Watershed: Monitoring, Activity Measurement, and Quantification of Adverse Effects.

1. Does the proposal include a detailed budget for each year of requested support?

   XYes -No

   If no, please explain:

2. Does the proposal include a detailed budget for each task identified?

   XYes -No

   If no, please explain:

3. Does the proposal clearly state the type of expenses encompassed in indirect rates or overhead costs?

   XYes -No

   If no, please explain:

4. Are appropriate project management costs clearly identified?

   XYes -No

   If no, please explain:

5. Do the total funds requested (Form I, Question 17A) equal the combined total annual costs in the budget summary?

   XYes -No

   If no, please explain (for example, are costs to be reimbursed by cost share funds included in the budget summary).

   Federal funds.

6. Does the budget justification adequately explain major expenses?

   XYes -No

If no, please explain:

7. Are there other budget issues that warrant consideration?

   -Yes **X**No

   If yes, please explain:

Other Comments: