PROGRAM REVIEW
DIVISION OF MICROBIOLOGY
FDA, NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH
SITE VISIT REPORT
JULY 23 – 25, 2007

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Report to NCTR Administration and Science Advisory Board:

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General comments:

Dr. Cerniglia has built a comprehensive team of scientists to address many important topics with both the Federal Drug Administration (FDA) and the public. The committee commends the talented scientific leadership and strong administrative skills of Dr.Cerniglia. Research topics to be addressed include:

- Food Biosecurity, Food Safety, and Methods Development
- Antimicrobial Resistance
- Gastrointestinal Microbiology and Host Interactions
- Environmental Biotechnology

The 13 Microbiology Division Principal Investigators (PIs) need to be commended for publishing in high-quality journals, with a range of 19 to 24 refereed publications per year. They are working hard to produce high-quality journal articles rather than producing as many publications as possible. Their research activities seem relevant to the FDA strategic plan, while maintaining a high level of research diversity within the division, with some cross fertilization into other FDA programs (Table 1). New hires since the last review include Rajesh Nayak, Huizhong Chen, Christopher Elkins, Kidon Sung, Mark Hart, and Seong-Jae Kim. These new hires were brought in to replace retiring individuals and to fill new positions created for homeland defense. The Principal Investigators are encouraged to continue seeking support from the counter terrorism

funds. Dr. Cerniglia is encouraged to fill the surveillance support staff position vacancy ASAP. It is our understanding that the much needed mass spectroscopy support position has been filled.

Project relevance to the FDA was an important topic of discussion for the review team. Dr Cerniglia explained that the project approval process includes a concept paper and a description of the research's contribution to FDA goals. Once approved internally, a full proposal is drafted. The research topic's relevance to the FDA is described in the Microbiology Division Executive Summary section (Table 1 of the review document) and the Contribution of FDA's Strategic Goals (pages 28-38 of report) section. Table 1 is a metric we constructed, which summarizes the relationship between the research topics and the FDA strategic goals and objectives.

Recommendations:

Adequate support staff and supply funds are not available to this division. More discretionary funds for each Principal Investigator are necessary (i.e., laboratory supplies, expendables in the order of $20-25K per year). For example, the NIH standard for supply funds is in the $20-25K range. A continued lack of fiscal support will jeopardize the overall quality of research. We encourage Dr. Slikker to continue to seek additional funding for this division.

Likewise, the review team believes that high-impact research needs more permanent support staff. Since several PIs do not have ORISE Post-Docs, we would like to see them supported, especially those in the Food Safety/Food Biodefense arena (Ashraf Khan, Saeed Khan, and Mohamed Nawaz). The ideal situation would be to provide each PI with a technician, post doc and student. Since the technicians have both great salaries and working environments, they rarely leave, which provides PIs the benefit of long-term support staff. Long-term staff keeps the continuity and ensures easy flow of skills and operations.

The debuty director position still has not been addressed, which was a recommendation from the last review. It would be very difficult to replace Dr. Cerniglia visionary leadership and organizational skills. Therefore, succession planning should occur within the next review cycle. Dr. Pain, team leader of the Surveillance Program, is eligible for retirement, and continuity in skills and leadership is needed there also.
We advise the PI to move away from possible hazard to relevant risk for each of the projects.

One challenge the Division of Microbiology faces is lack of scientific exchange with FDA Centers/ORA. We would encourage the division to do the following: (a) develop a plan for communicating research projects and conclusions with FDA Centers/ORA, (b) pursue additional formal collaborations with scientists in FDA Centers/ORA, and (c) explore the mechanisms by which their research programs could influence FDA regulatory policy and programs. One suggestion would be to run a jointly funded pilot

program with CFSAN to work on standard methods to recover bacterial and viral pathogens from fresh produce, particularly leafy green vegetables.

FDA Centers develop and issue assignments to the field (ORA) based on research studies, risk studies, and in response to emerging issues. How will research at the NCTR help establish priorities in these program assignments? Conversely, how will research conducted at other centers, especially CVM and CFSAN, integrate with and guide division activities so as to fill important knowledge gaps?

Some future directions:

The development and validation of standardized methods is critical for FDA regulatory science. FDA regulatory labs must establish and document the accuracy, sensitivity, specificity, and reproducibility of test methods. The expertise in the division can be an extremely valuable component of collaborations with CFSAN, CVM, and ORA method development and validation studies. It is recommended that the division pursue leading, participating, and advising in development and collaborative studies of regulatory methods.

Food safety research for produce foods (fruit, vegetables, salad crops, etc.) needs to be increased, as this is a growing area of concern for the public. Unlike other food groups, many produces do not receive a heat step prior to eating.

We suggest recruiting a senior microbiologist in the food safety arena with a background in enteroviruses.

To improve communications among the different FDA centers, we recommend a seminar series where once each week a PI from one of the centers gives a research seminar that is available via two-way web communication or via telecon. For both processes, everyone participating receives a PowerPoint file to view from their computer during the seminar. It can also be performed in a conference room around a PowerPoint projector.

There needs to be a greater focus on risk assessment to decide which projects to do. Likewise, for how they do their assays there is a need for assessing the risk, intervention points, critical control points, environmental elements, technology transfer, and standardizing methods. What are the usable results that will help FDA in the field? Unfortunately, help with these relevant issues has been difficult to achieve due to a poor response from colleagues within the FDA. FDA Centers develop and issue assignments to the field (ORA) based on research studies, risk studies, and in response to emerging issues. How might work at NCTR help in setting priorities in these program assignments? Conversely, how might research conducted at centers, especially CVM and CFSAN, integrate with and guide division activities so as to fill important knowledge gaps?

Specific comments:

Surveillance Program

Strengths and recommendations:
This program is highly important, not only for the division but also for the larger NCTR community. The major concern with this program is the vacancies/lack of support staff. The Surveillance Microbiology Program is a bit at a crossroads in terms of staffing - they need one additional person that could do both research and surveillance. It may also be a good time to consider contracting out this service (Don Paine is eligible to retire). The program already contracts out the Virology/Serology Service to the University of Missouri. What is left is the Bacteriology Service. Organizationally speaking, the Surveillance Program could stay in the Division of Microbiology or be moved to the Veterinary Services Program at the NCTR. This would eliminate the issue of the research program discretionary budget underwriting some of the costs for surveillance, which is an NCTR center-wide function.

Food Biosecurity, Food Safety, and Methods Development

Strengths:
This program has done interesting work on the effects of egg white lysozyme on *B. anthracis* at the request of Homeland Security via FSIS –USDA , establishing an excellent collaborative relationship with FSIS-USDA in the process The microarray assay with ability to detect 50 difference antibiotic resistant markers gave interesting results for *Staphyloccus* and *Enterococcus* isolates, but this program needs to consider doing comparisons of food versus clinical isolates to establish trends in levels of antibiotic resistance. The finding that a simple boiling of samples for RNA preparation with Triton X-100 was superior to the commercial kit RNA preparation procedures is useful. The survivability of *Bacillus anthracis* spores in various egg products has obvious model research value for homeland defense needs. Likewise, the finding that the egg white fraction prevented growth and survival of these spores, likely due to the presence of active lysozyme, is important but not an entirely new finding for susceptibility of Gram positive bacteria for which this phenomenon has been known for a long time.

The program established a good collaborative relationship with University of West Virginia poultry farm for research. The program also secured cooperation and involvement of multiple federal agencies in looking at an important topic, the persistence of particular serotypes of *Salmonella*, here *S. enterica* serovar Javiana, in multiple flocks grown on the same Virginia farm. Collaborative relationships were also established with the FDA-CFSAN and FDA-CVM as well as the USDA-ARS for microarray biochip evaluations (developed at the USDA-ARS). This research team evaluated a microarray biochip to detect virulence and antimicrobial-resistant genes of poultry and tomato serovars of *Salmonella* which provides information to build an important database for homeland/bioterrorism defense. Works on *Salmonella enterica* serovar Heidelberg using Pulse Filed Gel Electrophoresis (PFGE) is interesting work, especially showing that

resistance to streptomycin and gentamicin can be transferred among strains by mobile genetic elements. The work on *Salmonella enterica* serovar Javiana is important, because this serovar has been associated with recent human salmonellosis cases contracted from consumption of raw sliced Roma tomatoes. More information is needed to understand what the natural reservoirs and alternate reservoirs for such serovars are in nature. This work shows that there was a three fold higher level of antibiotic resistance and resistance to more antibiotics for the food/animal isolates (112 strains) than that for the clinical isolates (144 strains) tested.

Weaknesses:
The program needs to be careful about any claims of a unique approach of lysozyme, since much has been published earlier about the ability of this enzyme to trigger spore germination and outgrowth for Gram- positive bacteria. On *Salmonella* antibiotic resistance of isolates from imported seafood, the program needs to first establish that this food source has been a major source of foodborne illness - evidence of which we are not sure exists (i.e., a risk-based approach to prioritizing research). On this second project, the program should consider the effects of exposure of *Salmonella* strains to 3 % salt on gene expression. Another perhaps more relevant project might be the incidence of antibiotic-resistant spoilage and pathogenic bacteria on farm-raised catfish in the United States. The researcher needs to show publications in refereed journals in his reports for site review and consider initiating additional active collaborations with other labs off campus.

Unequivocal tests in a grow-out area requires quarantine of air, insect, and other animal movement between research plots. A control to consider in the experimental design is a split plot with the same bird type for all treatments, but use no antibiotic plus usual coccidiostats for one set, and a second set of birds with antibiotics and usual coccidostats. Look for persistence of antibiotic resistance in both sets. (Note: work on swine *Salmonella* isolates at University of Kentucky research farm indicates persistence of *Salmonella* types even after removal of antibiotics for management scheme.) Consider monitoring dynamics of *Salmonella* isolates as function of age, two-to-three-week-old poultry vs. harvest age of 22 weeks. Watch for confounding effects of genome drift in target *Salmonella* strains as function of time on farm as this can confuse the PFGE pattern interpretations. Also, streptomycin and gentamicin are not important for treating salmonellosis. The PFGE work is duplicative of the NARMS program which has tested many more *S.* Heidelberg strains.

Ability to achieve research objectives:
Science for the anthrax project is sound but researchers should consider whether lysozyme will work in real-world food products with acid or alkaline pH values that would allow survival and infectivity of *B. anthracisis* spores while inactivating much of the lysozyme? A question relating to the toxicology to humans is what is the effect of airborne lysozyme on human lungs, etc.? No duplication to other centers is known. This project is very relevant to FDA goals and homeland security. It may also lead to new technologies to protect the public. This project is in collaboration with the Department of Homeland Security.

Science for the poultry project is sound with some duplication with other centers. The project is very relevant to FDA goals and to food safety/security. The interaction with other federal agencies is great.

Research recommendations:
General suggestion for anthrax and poultry project: PI should consider expanding the base of work to include working with other PIs on the bigger picture. There is a question as to how environmental stresses of elevated temperatures, decreased pH, and other factors will affect the level of expression of the antibiotic-resistant genes and of virulence genes. Microarray data has the most utility and meaning when it is tied to whole-cell physiological conditions the pathogens are exposed to in real-world conditions. Work toward expression microarrays would be a useful approach. While detection of antibiotic resistance spread is essential, quantitative assessments would be useful to developing approaches for risk management.

Antimicrobial Resistance

1. *Role of bacterial efflux pump on resistance:*

Strengths:
The basic research work on efflux is "cutting edge" and is resulting in important contributions to our understanding of the role of efflux pumps in both resistance and bacterial physiology. It is clear that efflux pump inhibitors, if safe and effective, would be a major advancement in anti-infective therapy.

Recommendations:
The researchers are encouraged to identify additional aspects of this research to fill data gaps relevant to regulatory issues. One suggestion is to perform the *AcrAB* studies in *Salmonella typhimurium* or *S. enteritidis*, with comparisons among other serovars and foodborne enteric pathogens. The *AcrAB* efflux pump is associated with β-lactam antibiotic resistance. Also, apply microarrays to study expression changes following exposure to clinically relevant antimicrobial agents.

2. *Microarry research:*

Strengths:
The work on the microarray with USDA is a logical method development approach and is leading to novel findings. These discretionary tools are very powerful.

Weaknesses:
The link between pre-harvest *Salmonella* in turkeys and counter-terrorism was not well made. The pre-harvest turkey study did not identify the source of *S.* Heidelberg and did not explain why positive pens became negative or whether the spread was due to multiple introductions. It seems that the array needs more controls. How these tools can be used for biosecurity surveillance needs to be expanded. This is an important area of research.

3. *Bacterial contaminated feed research:*

Strengths:
Studies to characterize *E. coli* and *Salmonella* from feeds and animals have clear benefits to the FDA. The methods applied are appropriate. *Salmonella* strain typing for seafood is a new procedure for tracking intentional and non-intentional foodborne outbreaks.

Weaknesses:
It was less clear how the information on the salmonellae from seafood would be used to assist the FDA. There were some technical questions on the orange juice studies, such as the strategy to use PCR to look for the *flo* and *int* in strains that lacked the corresponding phenotypes.

4. *Tetracycline resistance in Aeromonas from catfish :*

Strengths:
Technically sound and thorough.

Weaknesses:
There was concern about the decision, in the face of limited resources, to focus on tetracycline resistance in *Aeromonas* from catfish. Neither the human nor the veterinary health hazards posed in tetracycline resistance in this genus was made clear, nor was the importance to the FDA mission.

Recommendations:
We suggest rethinking the research direction or refining the current studies to address public health priorities. We recommend the researchers move away from tetracycline to fluoroquinolones.

5. *Biodegradation of ceftiofur:*

Strengths:
Biodegradation of ceftiofur is an example of the division's biggest strength in an area of primary importance to the FDA/CVM mission, both in terms of the environmental fate of antibiotics and for the selection pressure place on foodborne pathogens, where cephalosporin resistance is a high priority. Pfizer found it was rapidly degraded by the bovine flora. NCTR interests are to characterize its degradation process.

Recommendations:
The division should take full advantage of their expertise in this area and continue to apply their considerable skills to address important public health concerns.

6. *Probiotic influence on intestinal health and competitive exclusion:*

Strengths:
While not directly related to antibiotic resistance, the work on probiotics, if successful, can reduce our reliance on therapeutic interventions. Much remains to be learned about probiotics and their ability to influence intestinal health and exclude colonization by fecal pathogens.

Recommendations:
We encourage the researchers to extend the probiotic prevention studies to *Campylobacter* in poultry. This is a complex problem that needs more interaction with other NCTR PI and other FDA centers. Seek out some CRADA, since the industry is also interested in probiotics.

7. *Vancomycin-resistant Enterococci:*

Strengths:
With difficulty getting other some primers to work, they are producing their own primers.

Weaknesses:
As noted elsewhere, we believe it is important that epidemiology and risk analysis play an important role in the prioritization of NCTR research. The spread of VRE via food animals is not a major public health issue in the United States, where glycopeptides have never been used in food animal husbandry. In addition, the typing scheme used to characterize the isolates was devised *de novo*, despite the availability of established schemes for typing the van gene cluster in clinical isolates; and it appears that no attempt was made to compare techniques. We question the current relevance to FDA's research needs.

Recommendations:
Need some guidance from CDER. We agree with moving to *Campylobacter,* which is a growing problem.

8. *Staphylococcus aureus antibiotic resistance:*

Strengths:
Staphylococcus aureus methicillin resistance is fatal in healthy individuals. Proteomic studies demonstrated 541 unique protein expressions within 24-hourincubation. Bacterial hyaluronidase is an important invasive enzyme toward human infection. The researchers are proposing to produce hyaluronidase knock-out to determine if this enzyme is important for virulence. Hyaluronidase is a virulence factor for *Streptococcus*.

Recommendations:
Is anyone evaluating heat stable virulence factor in staph as a virulence factor? There are 17 serotypes of Staph enterotoxin. Which proteins are relevant? The protein structure function issue is relevant. This research is very good and very important.

Gastrointestinal Microbiology and Host Interactions

Strengths:
We complement the investigators on the breadth of their expertise and the applicability of their research programs to aid in addressing safety questions and issues. The scientists of the Microbiology Division are a resource in developing a variety of *in vivo* (gnotobiotic, germ- free, target animal) and *in vitro* model systems (e.g., fecal batch culture, fecal semi-continuous cultures, intestinal epithelial model) and methodologies to examine the effects of exogenous compounds (antimicrobial agents and their residues, probiotics, food and feed additives,) and endogenous host-derived factors on the GI microflora and the host immune system. The scientists work collaboratively within the division, a strength that continues to enable them to leverage the broad expanse of microbiological, biochemical, molecular, and other technological expertise that they and their colleagues have applied and are currently applying to different safety, metabolism, and degradation questions presented in the review. These scientists are contributing to our basic understanding of the bacterial metabolism and host interactions of exogenous and endogenous substrates they have selected for study. Their expertise is recognized outside of the NCTR, as they are now beginning to obtain external funding (e.g., CRADA funding from Pfizer, Project Awards from the Office of Women's Health). They are also serving in an advisory capacity for issues associated with safety/efficacy of probiotic use in animals and in people, including safety of drug residue ingestion and metabolism of substrates such as plant hormones, azo dyes, food additives, and supplements. The scientists have a solid publication record.

Weaknesses:
Scientists are encouraged to evaluate the variability, reproducibility, and predictive value of the model systems used in addressing human-safety questions and the risks of identified hazards. As the scientists are working in an advisory capacity, the issue of the applicability of the model systems in predicting effects on humans and decisions on public health safety becomes more important in applying their experimental work in context of any safety recommendations (see below on recommended work).

Ability to achieve research objectives:

The budget could change dramatically, given past history, increasing the need for scientists to seek and successfully obtain extramural funding, and it appears that these investigators are indeed actively seeking funding.

The studies of ceftiofur metabolite identification need stronger analytical support (i.e., more analyst time) to advance the project and may need labeled ceftiofur.

Research recommendations:
Recognizing that the germ-free mouse and human flora-associated mouse models are resource intensive, we recommend that future studies take into consideration the following questions:

- In colonization succession studies of germ-free mice inoculated with human fecal flora: Do the high levels of enterococci and clostridia (compared to *Bifidobacteria* and *Bacteroides*) on day 14 post inoculation occur in all mice similarly inoculated? The comparatively high levels of enterococci compared to other organisms would not be expected on average in fecal samples from adult humans. Does this affect the interpretation of the results in terms of human safety? Is the colonization progression shown in the PowerPoint slides comparable (in terms of changing percentages of organisms) from one experiment to another, or to other human-flora associated models? Is this progression at day 14 representative of human flora? When probiotic studies are conducted, do the changing levels of bacterial groups affect the interpretation of experiments (e.g., in the *Salmonella* and *Campylobacter* challenge studies)? Would the same results occur if the challenges occurred on day 14 rather than 7? Perhaps a statistician could aid in future experimental designs, incorporating data from earlier experiments.

- Are there other models/studies that corroborate/validate the observations made in the studies of the probiotic effects on pathogen colonization of the mice? For example, reproducible models of *Campylobacter* colonization in mice are lacking[1]. Is the mouse an appropriate model to study colonization resistance (of human microflora) for *Campylobacter* that can be translated to human-host response? Is there evidence elsewhere that the probiotic used inhibited the immune response in other animals' models or humans? Was the response representative of what is observed in humans or other animals? Does the probiotic colonization of mice mimic that observed in humans? If not, or no information is available, then why is this model predictive /applicable to safety decisions in humans?

- The *Clostridium* studies provide molecular information on fluoroquinolone resistance where basic information is lacking. Have attempts been made to determine whether fluoroquinolone-resistant, clinical (diagnostic) isolates from humans (hospital or community-acquired) or animals (e.g., poultry isolates that may be obtained via the USDA collaboration) have the same mutations as those documented in the laboratory strains? If the mutations are the same in clinical (field) isolates and those generated in the laboratory, such information would provide a rationale for further investigational studies of the laboratory strains and expression of virulence determinants. Comparisons could be made between the isogenic lab strains as well as fluoroquinolone resistant, clinical isolates that have the same (or different) mutations. How prevalent are such mutants among clinical isolates in humans? If prevalence is low, or the mutations in the lab isolates versus clinical isolates were different, what would be the prioritization/emphasis of future studies on the laboratory strains?

- Given that the division has developed and has expertise in more than one intestinal model (*in vivo* and *in vitro*) and that it is difficult to validate these

[1] Chang, Miller. *C. jejun*i colonization of mice with limited enteric flora. I&I 2006; 74:5261-71

models for purposes of evaluating human safety questions addressed by the FDA, is it possible to examine the effects of molecules in different models and determine whether the observations (e.g., no-effect concentrations, determinations of changes in colonization barriers, metabolic fate, etc.) are similar in different models? Are the observations reproducible within a model? If the answer is unknown or no for either of these questions, then what is the justification for their use in risk assessments for safety of exposure to test molecules? Are the models predicting no-effect concentrations that are higher or lower than would be expected in humans?

Environmental Biotechnology

Overview:
Two projects were reviewed by the SAB as part of the Environmental Biotechnology focus area: Microbial Transformation of Fluoroquinolone Antimicrobial Agents and Elucidation of Biodegradative Pathway for High Molecular Weight Polycyclic Aromatic Hydrocarbons. The first project focused on the identity of biotransformation products formed by pure fungal and bacterial cultures as well as a mixed activated sludge culture. The second related to elucidating the full pathway, including the genes and enzymes for pyrene and fluoranthene by pure cultures of *Mycobacterium*.

In the case of both projects, the science was sound and original. The first project demonstrated that microorganisms from and in the environment are capable of biotransforming fluoroquinolone antimicrobial agents and provides an indication of the identity and antimicrobial properties of metabolites, which may be present in environment. The second project resulted in the most comprehensive elucidation to date of the full pathway for PAH degradation by a bacterium.

Microbial Metabolism of Fluoroquinolone Drugs

Strengths:
This work shows the potential for fluoroquinolone drugs to undergo microbial biotransformation, and resulted in the identification of potential metabolites, which might be present in the environment. This is new information for assessing the fate of these drugs in the environment.

Weaknesses:
The work to date focuses on the use of pure cultures and a grab sample of liquor from a sewage treatment plant. All studies have been done at relatively high concentrations, which facilitate the analytical chemistry, but may not reflect what occurs *in situ*. This work should be viewed as a first step and a move should be made into more realistic systems simulating the actual environment to provide a more accurate picture of the kinetics and extent of metabolism occurring *in situ*.

Elucidation of PAH Pathways

Strengths:
This works represents an unparalleled application of genomic, proteonomic, and analytical chemical approaches to document the bacterial biodegradative pathway for a xenobiotic. The completion of this project represents a major achievement in microbial physiology. The quality of this work is validated in the nature of the journals in which it has been published.

Weaknesses:
There is not a transparent link between this work and FDA's mission. However, the work is well funded by EPA and DOE and additional support has been requested from NSF and the Arkansas Biological Institute. The techniques and capabilities developed as a result of this work may have application to future work needed by the FDA.

Prospectus and recommendations for the future:
Since the last review, there has been growing awareness and concern regarding the development of antimicrobial-resistant microbes in the natural environment. Both antimicrobial agents and microbes resistant to antimicrobials have been detected in natural environments. In general, these antimicrobial agents have been observed at very low, non-therapeutic concentrations. A key challenge for the future is to determine whether concentrations present in the environment actually contribute to the development or maintenance of resistance there within. Such understanding will be essential for quantifying the actual risk associated with antimicrobial agents in the environment. Important knowledge to manage this challenge will include a better understanding of the full fate of antimicrobial agents released to the environment, including half-lives of parent compounds and their metabolites and their bioavailability and ability to select for resistance under real-world conditions.

Another growing issue is the widespread presence of pharmaceuticals in the environment and their potential effects. The importance of this issue is reflected by the recent U.S. Geological Survey work determining the presence of a diverse array of pharmaceuticals in U. S. surface waters and increasing reports of feminized fish below wastewater treatment plants associated with synthetic hormones used for birth control and other purposes. NCTR is uniquely qualified within the FDA and other government agencies to understand the fate of pharmaceuticals in the environment and explore real biotechnological solutions to improve their biological removal during wastewater treatment. This goal can be achieved by leveraging existing competence in biochemistry and microbiology to better understand degradation kinetics under actual conditions in the field. This will require a shift in emphasis from pure culture studies to more realistic fieldwork studies with mixed cultures as they occur in nature.

Metrics summarizing the Microbiology Division research topics' relevance to the FDA Strategic Goals and projects with collaborating federal agency/center (page 28 to 38 in the report).

Program/Research topic	Principal Investigator PI	Relevant FDA Strategic goal statement and objective number Goal 1	Goal 2	Goal 3	Collaborating U.S. Agency/Center
Food Biosecurity, Food Safety, & Method Development					
1) Biochip for *Salmonella* serovars virulence genes	Rajesh Nayak		2.1		CFSAN
2) Bacterial finger printing for poultry	Rajesh Nayak		2.1	3.1	USDA CVM
3) Seafood gene chip development of antibiotic resistant bacteria	Ashraf Khan			3.2	ORA CFSAN
4) Isolation and characterization of Salmonella from imported seafood.	Ashraf Khan		2.1		ORA
5) Aquaculture/ catfish as a reservoir for tetracycline resistant *Aeromonas veronii*	Mohamed Nawaz			3.1	CVM ORA
6) Study the growth and inactivation of *Bacillus anthracis* in liquid egg products	Saeed Khan		2.1	3.2	DHHS, APHIS, USDA, DHS
Antimicrobial Resistance					
1) Develop new antimicrobial susceptibility methods	Rajesh Nayak		2.1		ORA CFSAN CVM
2) Mechanism for vanocmycin resistant enterococci (VRE) development	Kidon Sung Saeed Khan		2.1	3.1	CVM
3) Identify novel proteins in antibiotic resistant *S. aureus*	Mark Hart		2.1		
4) Efflux pump deficient bacterial mutant development and characterization	Chris Elkins		2.1		
5) Antimicrobial resistance Microarray biochip	Rajesh Nayak		2.1		USDA

Gastrointestinal Microbiology and Host Interactions				
1) Steroid compound can influence the resistance phenotype of commensal bacteria in GI tract or transient pathogens	Chris Elkins		3.2	
2) Understanding how drug resistance or xenobiotics substances effect microbial flora and how changes affect human health	Fatemeh Raffi	2.2 & 2.3		USDA
3) *In vitro* competitive exclusion (CE) assay for assessing new antimicrobials	Doug Wagner	2.3		CVM
4) Documenting the transfer of resistance genes among genera and other bacteria	Doug Wagner	2.3	3.1	CVM
5) Cell culture based assay sensitivity to determine drug resistant bacterial populations in animal intestine	Doug Wagner	2.3	3.2	CVM
6) Biological effect of probiotics on human immune system	Doug Wagner	2.1	2.3	CVM CFSAN
7) Vaginal probiotic efficacy, potency, and safety as to if Lactobacillus can thwart *Staphylococcus aureus* growth, SST-1 toxin production in women tampons	Chris Elkins and Mark Hart	2.1 & 2.3		OWH
8) Metabolism of azo dyes (tattoos) by the skin and intestinal microflora	Huizhong Chen	2.3	3.2	CFSAN
9) Biodegradation of Sudan dyes found in contaminated food by intestinal microflora	Huizhong Chen		3.2	CFSAN
10) Determine the mechanism of inactivation and degradation of third generation cephalosporins by the bovine intestinal microflora	Bruce Erickson	2.3	3.2	PFIZER CRADA

11) Development of rapid and sensitive molecular detection methods for intestinal bacteria	Huizhong Chen Carl E. Cerniglia		3.1	CVM
Environmental Biotechnology				
1) Metabolic, genomic and proteomic approaches in elucidating the metabolic pathway of polycyclic aromatic hydrocarbon (PAH) degradation by microorganisms and mammalian enzymes	Seong-Jae Kim Carl E. Cerniglia	1.3	3.2	EPA DOE CVM
2) Persistence of fluoroquinolone antimicrobial agents in the environment	John Sutherland	1.1	3.2	CVM

CFSAN – Center for Food Safety and Applied Nutrition
CVM – Center for Veterinary Medicine
DHHS – Department of Health and Human Services
DHS – Department of Homeland Security
DOE – Department of Energy
EPA – Environmental Protection Agency
ORA – Office of Regulatory Affairs
OWH – Office of Women's Health
USDA – United States Department of Agriculture

FDA Strategic Goals Summary (Page 28, tab 1, Microbiology Division Report)

Goal 1: Enhance Patient and Consumer Protection and Empower Them with Better Information about Regulated Products
Objective 1.1: Improve safe and effective use of medical products with better information technology and effective risk/benefit communication.
Objective 1.2: Increase ability of consumers to make food choices and to sue food handling practices associated with health benefits and reduced risk.
Objective 1.3: Improve the infrastructure for problem detection and product information dissemination, to strengthen consumer protection and take timely effective risk management actions with all FDA-regulated products.

Goal 2: Increase Access to Innovative Products and Technologies to Improve Health
Objective 2.1: Increase the number of safe and effective new products available to patients, including products for unmet medical and public health needs, emerging infectious diseases and counterterrorism.
Objective 2.2: Sustain access of safe and effective new products by improving rapid, transparent, and predictable science-based review of marketing applications.
Objective 2.3: Increase access to safe and effective veterinary products, and to safe and nutritious food products, including products for unmet animal and human health needs.

Goal 3: Improving Product Quality, Safety, and Availability through Better Manufacturing
Objective 3.1: Maximize product quality, safety, and availability, by encouraging use of improved manufacturing technologies and product characterization techniques.
Objective 3.2: Prevent harm from regulated products by increasing the likelihood of detection and interception of substandard manufacturing processes and products through efficient and effective risk targeting, external partnering, effective internal processes, and collaboration.