

**Animal Genome Reagents and Tools: Species Priorities** July 13, 2005

*Submitted by National Animal Genome Research Program (NAGRP) Coordinators on behalf of the NAGRP/NRSP-8 Committee membership:*

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On Feb. 15 of this year, we submitted a letter to indicate our concern regarding the announced plan to sunset National Research Initiative Program 43.1, Animal Genome Reagent and Tool Development, in FY 2006. We were extremely gratified to receive a response from Dr. Palmisano on Feb. 25, indicating that some version of this program would continue but in a redesigned and refocused form, beginning with the FY 2006 NRI RFA. We agree that the recently completed draft sequences of the chicken and bovine genomes, along with the anticipated sequence of the swine genome, provide good reasons to rethink the needs of animal agriculture. That letter also requested additional input that might assist CSREES in prioritizing future resource commitments. This response to Dr. Palmisano is submitted by the NRSP-8 species coordinators after consultation with the NRSP-8 species committees.

**Status of sequences:** As shown in the attached Table I, draft sequences are presently available for the chicken and cattle genomes, and, with continued leadership from USDA, we anticipate a similar level of coverage of the swine genome will be available in the next two years. The sequences are in various stages of assembly and annotation, but all three will require some level of “finishing” to fill gaps, correct errors and address missing genes. Whether this is done in a central, concerted fashion or by individual, isolated efforts (or both) remains to be seen, but the “draft” status of these sequences should be kept in mind. (Picture a novel with no spaces or punctuation and some pages left out or misplaced). Other important agricultural genomes (sheep, horse, turkey and several aquaculture species) are unlikely to be fully sequenced in the near future, but important advances will occur with investments in tools for these species as well. For example, high resolution sheep-cow comparative maps allow sheep geneticists to benefit almost as much from the bovine sequence as do cow geneticists. Comparative maps for these species will require BAC contig maps aligned to the reference sequence, along with dense EST coverage.

**Priorities:** For those species with sequenced or soon-to-be-sequenced genomes, the most important tools are those that allow researchers to utilize the sequence. Thus, a top priority in these species is to develop **high density polymorphism (SNP) maps and genotyping technology** that lead to the identification of key quantitative trait loci that govern agricultural animal health and productivity. These tools will translate the draft sequences into knowledge that directly can be applied to breeding. A second priority is **development of bioinformatics tools** that allow sequence and related SNP and expression data to be shared and understood by both basic scientists and user communities. A third priority is to look beyond DNA sequence at gene expression changes that ultimately govern phenotypes. Generally speaking, this is the realm of **“functional genomics”**. Many efforts have already been made along these lines (e.g., microarrays), but critical needs remain for **proteomics reagents** (high throughput expression and two-hybrid libraries and monoclonal antibody libraries, mass spectrometry tools), and **high throughput mutagenesis strategies** (RNAi, transgenic technology). In particular, there’s a need for well-characterized bovine cell lines for transfection and RNAi studies, and, in poultry and several other species, there’s a need for stem cell lines for more efficient generation of transgenic animals, including targeted

gene replacement and RNAi approaches. There's also a demand for maintenance of existing mutant lines, developed based on naturally occurring mutations (often cumbersome and/or expensive in larger animals).

As noted above, for those agricultural animals that lack genome sequences, the **top priority will often be comparative BAC contig maps (integrated with available linkage maps), skim sequencing and/or EST development that allow alignment of the genes of those species along the platform of a related reference sequence** ("one sequence, multiple genomes"). It's important to note that such comparative approaches not only benefit the "unsequenced" species but are of great value in the annotation and understanding of the reference species itself. Furthermore, agricultural phenotypes studied in the unsequenced species will often be of relevance to the biology of the reference species. Such comparative linkages also allow groups of species, rather than just a single species, to benefit from the SNPs, bioinformatics and functional genomics advances prioritized above.

Thank you for the opportunity to provide this input, and we hope that CSREES finds these comments to be of value. Genomics technology advances very rapidly and will likely offer additional, unforeseen opportunities in the not too distant future. Also, there will always be individual differences of opinion in the priorities for individual technologies and individual species. These differences can best be resolved by CSREES peer review panels that have long been the cornerstone for fair and cost-effective allocation of NRI funds. We continue to be available to assist in planning for future research in animal agriculture.