Bob Hendon,
CSU Purchasing

Dear Bob,

Macromolecular Resources, the life sciences core laboratory for Colorado State University, wishes to upgrade its DNA sequencing capability by replacing an old-generation instrument with new technology. I would like to request a waiver of the bid process for the purchase of a new DNA sequencer instrument. Neither I nor any other staff member at this facility has any conflict of interest related to any vendor of this type of equipment. As far as I know, there is only one commercially available instrument that meets all of our needs for enhancing the performance, throughput and flexibility of our DNA sequencing operation and the service we can provide to the CSU research community. The necessary features and their availability on various instruments are detailed below.

The old technology depends on using a slab gel to separate DNA components, and a fresh gel must be prepared each day that samples are run. Preparing such a gel takes several hours before samples can be run and involves handling toxic chemicals, most notably acrylamide. Once the gel analysis procedure has been completed, usually in an overnight run, we have raw data that are distorted by gel imperfections, and it is necessary for the technician to perform a painstaking manual procedure called "tracking the gel" before automated procedures can by employed to interpret the data as a DNA sequence. Detecting the DNA components in the gel is based on observing light of several different colors from several fluorescent chemical labels added to different DNA types. Our old instrument accomplishes this by using a set of optical filters mounted in a moving wheel and making one measurement for each color for each DNA type. The colors associated with different DNA types overlap and the filters necessarily reduce the amount of light available to the detector, so measurements are not as specific as we would like and light loss means reduced sensitivity. In addition, as improvements are made to the chemical procedures of DNA sequencing, the light colors change and the instrument must be updated by replacing the mechanical filter assembly.

The preferred instrument incorporates two critical technology advances which are key to meeting the requirements. First is the shift away from the slab gel principle of operation to the much superior "capillary electrophoresis" principle. Capillary electrophoresis operates in a fully automated manner, eliminating the need to prepare gels and handle toxic acrylamide, thus significantly simplifying and expediting the overall analysis. Capillary electrophoresis is inherently a higher performance analytical technology than is gel electrophoresis, offering both better sensitivity and higher resolution. To the end user, who wants to have as much information as possible about the sequence of his DNA sample, this means data which are more useful because the accuracy of the sequence determination and the length of sequence that is characterized are both increased. Raw data from capillary electrophoresis are also directly amenable to automated interpretation, which eliminates the manual tracking step with its inherent error rate. Moving up to capillary electrophoresis provides throughput enhancement even more dramatic than the performance enhancement. For end users, obtaining more data in shorter time is an important convenience and a benefit to their overall project flexibility. Even apart from the hours gained by eliminating the effort of gel preparation and tracking, a 16-capillary system can run roughly twice as many samples in a 24 hour period as can a slab gel system. Furthermore, gel tracking must be done for all samples at the end of the run, so no data for any sample are available until the next day. With 16-channel capillary electrophoresis, data for 16 samples are available within about 2 hours.

A second major technology advance is the replacement of fixed wavelength optical filters in the detection section with full spectrum detection. Not having filters means better detection sensitivity. Obtaining full spectra means that the overlapping light colors are deconvoluted by software, which produces better overall instrument resolution. This improved light detection system complements both the sensitivity and the resolution performance gains as discussed above for the capillary electrophoresis technique. Using software rather than physical filters provides the flexibility we need to keep up when improved chemical labels and techniques become available, which occurs every few years. Only a simple software upgrade is needed to take advantage of progress in chemical procedures.

There are four known vendors of DNA sequencers: LiCor, Beckman/Coulter, Amersham/Pharmacia and Applied Biosystems. LiCor manufactures only the old-technology slab gel systems, so does not offer any advantage over the instrument we are replacing. Instrument cost is $60,000. Beckman ($90,000) offers capillary technology, but coupled with the less desirable fixed wavelength filter detection. Furthermore, the Beckman instrument runs only eight capillaries simultaneously, which would effect no improvement over our current instrument in the number of samples that can be run in a day. Amersham can be purchased with simultaneous operation of 16 or more capillaries, but still uses the fixed filter detection scheme. I have tried several times without success to obtain a price quote from Amersham. Their main office refers me to a sales rep. Three calls to the rep have contacted an answering machine and none have been returned. I even spoke personally at a trade show with an Amersham sales person who specializes in other products, and even that has not generated a call from anyone who can give me a price.

The ABI 3100 from Applied Biosystems ($116,000 including trade-in of our old instrument) does capillary electrophoresis with 16 capillaries simultaneously which will roughly double our daily sample capacity and improve turnaround time. It is the only commercial instrument with full spectrum detection. An important additional advantage is complete compatibility with the off-line software that both we and our clients are currently using to handle data after the initial processing. We are also familiar with the ABI service and technical support, which we find to be very good.

Sincerely,