CORRESPONDENCE

HEPATITIS B VACCINE IN YEAST

To the editor:

The article on "Mammalian Cell Culture: Worldwide Activities and Markets," (July '87) contains a factual error (in Table 1) that could negatively impact both our company image and our genetically engineered hepatitis B vaccine, "Engerix-B." This product is made in yeast cells and *not* in mammalian cell culture, as implied.

The cell substrate in which a vaccine is produced is a critical element in ensuring the product's safety. And yeast cells (*Saccharomyces cerevisiae*) are the only currently acceptable and internationally approved cells for rDNA hepatitis-B vaccine production.

Although many vaccine manufacturers work with mammalian cells (at the laboratory level or for producing diagnostic reagents), the use of mammalian cells as a substrate for vaccine production is still subject to clearance by international specialists, including the World Health Organization and international and national regulatory authorities.

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The title of the table in question is "Expected Dates of Product Introduction for Selected Products that *can* be made by Mammalian Cell Culture." I apologize if this may have given the impression that SmithKline's product is *actually* made by cell culture.

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MORE COMPETITION IN SEQUENCING

To the editor:

The article by Arthur Klausner on the DuPont automated DNA sequencer (*Bio/Technology* 5:1111, Nov. '87) gives an accurate description of fluorescent sequencers. We disagree, however, with the closing statement that users will have to choose between DuPont and Applied Biosystems for automated sequencing. In fact, the sequencing community will have a choice among three technologies for automated sequence acquisition: autoradiogram scanners, fluorescence detectors, and beta detectors. The latter two share the feature of collecting data while the gel is running: one detects fluorescent

emissions from primers or dideoxy nucleotides; the other detects beta emissions from conventionally radio-labeled fragments. Hitachi has announced a fluorescent scanner under development; Genofit and EG&G have announced plans to market beta scanners.

Bio-Rad, however, is convinced that the film-scanning approach provides much higher throughput and is more cost-effective than real-time systems. Our product is based on a highly sensitive CCD (charged coupled device) scanner that reads and processes conventional autoradiograms. This technology was demonstrated to be accurate and reliable in early 1986 (J. K. Elder, D. K. Green, and E. M. Southern, Automatic reading of DNA sequencing autoradiographs using a large format digital scanner, *Nucleic Acids Research* 14:417-424, 1986). Bases are assigned using pattern recognition and expert rules (e.g., detect compressions). The Bio-Rad product should be on the market at the same time as the DuPont unit, and will sell for half the price. Another firm claiming development of a scanner is Beckman.

A problem with the fluorescent systems, besides their high cost, is that the instruments are burdened with a 6-8-hour electrophoresis step. Data acquisition is very low during this stage. Our scanner, however, can potentially process films continuously, at the rate of 100,000 bases per day—5-10 times more than "real-time" systems. Fluorescent and beta detection systems also require 10 times the conventional amounts of DNA sample at extremely high purity to overcome signal-to-noise problems. Migrating bands only have a minute or so in front of a detector, whereas signal can build up over 12 hours with autoradiography. There is also the misconception that the gels are "automated" in the real-time systems. As it turns out, the same number of chemical reactions and gels must be run in either case. We simply use a 64-well comb (equivalent to 16 sequences on a fluorescence unit).

A further problem is that these real-time systems have no "back end" shotgun handler or DNA analysis programs; ours includes these to form an integrated package. Experts have told us that overlapping, editing, and verifying gel readings represent perhaps 50-90 percent of the

effort in the post gel running stage. We include the powerful Staden shotgun automatic overlapping and editing software with the autoreader because, after all, it is the consensus sequence that counts. Lastly, there is no hardcopy autorad to go back to with the fluorescence or beta detection systems, a shortcoming that hinders the verification process.

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WE MISSED ONE IN PLANT DIAGNOSTICS...

To the editor:

We were surprised that our company (formerly called Inotech Diagnostik AG) was not mentioned in the article "Immunoassays flourish in new markets" (*Bio/Technology* 3:551-556, June '87).

By 1980, we were already marketing ELISA reagents for the detection of viruses in potato, barley, grapevine, and onion. In 1982, we introduced the first commercially available monoclonal antibody in the plant diagnostic market. Since then, we have cooperated with Agdia, Inc. (Mishawaka, IN): Agdia is our exclusive distributor in the U.S. and Canada, and we represent Agdia in Europe.

F. Fux

Bioreba AG

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...AND ONE JAPANESE-EUROPEAN DEAL

To the editor:

Your articles on doing business in Japan (October '87) were particularly interesting, but I was dismayed to find no mention of the link between Carbohydrates International (CHI) and the Marubeni Corp. And this despite the fact that the arrangement of our close competitor Biocarb with the Mitsubishi Corp. was neatly featured.

CHI has had an agreement with Marubeni since April 1987 regarding the distribution of CHI's carbohydrate structures in the Japanese market. Currently, we are also actively pursuing collaborative research projects with a number of Japanese companies under our arrangement with Marubeni.

Keith A. Johnson

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