Sir: We would like to point out that in November 1988, before our paper was submitted for publication, a draft of our results was sent to BDH Ltd who market the Merck assay kit in the United Kingdom. The above letter to the *Annals of the Rheumatic Diseases* is the first response that we have received from Merck, however.

We do not dispute that many studies have been successfully performed within the past 10 years using the Merck polyomorphonuclear elastase kit. The only reservation that we have is when the assay is used with samples containing rheumatoid factor. Indeed, as described in our paper, we found no significant difference between results obtained with the Merck assay and those obtained with our *in-house* assay for control samples and samples from patients with seronegative spondarthritides. The only other published report which we have found which has investigated the possible interference of rheumatoid factor in the Merck elastase assay is that quoted in the above letter from Merck—namely, the paper by Neumeier, Fateh-Moghadam and Menzel.2 As scant methodological detail is provided in that paper, however, it is impossible for the reader to make any assessment about the statement that rheumatoid factor does not interfere with the assay.

The interference of rheumatoid factor in immunoaassays is well reported, and rheumatoid factors have been shown to bind to immunoglobulins from many species, including rabbit and sheep. As stated in the letter from Drs Heubner and Utz (Merck), the interference of rheumatoid factor in their assay would occur as the result of crosslinking antibodies to antigens—i.e., the antibody and the labelled detection antibody. However, contrary to their claim that this is ‘rather unlikely’, Elkon et al have shown that rheumatoid factor can bond both immobilised rabbit IgG and radiolabelled sheep IgG in the same assay.

The appropriate dilution buffers were used for each assay, and we did not find a protein matrix to be essential in our system. We do not claim that the additional incubation step which we performed in the *in-house* assay led to any increase in its sensitivity. The coating capacity in the ‘in-house’ assay was sufficient to produce a good signal-to-noise ratio to that obtained with the Merck assay, and after appropriate dilution synovial fluid samples containing elastase-α1 proteinase inhibitor at concentrations greater than 10 000 ng/ml were successfully measured. In a larger series of samples from patients with rheumatoid arthritis we have now found an increased range of plasma concentrations than in our previous report but still found that many measurements (about half) lie within the normal range.

We would dispute the claim made by Merck that the described fast protein liquid chromatography is of no value. Although we loaded more total protein than was recommended by Merck (the manufacturer) for optimial high resolution with the particular column, we obtained reproducible results. We did note a decreased resolution as reflected by the relatively large number of fractions needed to collect the peaks of interest and the narrow interval between the peaks. Owing to the large differences in molecular weight between the elastase complex and rheumatoid factor, however, we were still able to resolve these substances, as shown in our paper. This decrease in resolution, but still satisfactory separation of substances of these molecular weights, would be expected to occur under these conditions (source: Pharmacia).

The void volumes of between 7 and 9 ml for this column obtained by Pharmacia and Merck were also obtained in our experiments and in the 2 ml as stated in our paper. This misconception is entirely our fault as we omitted to state in the paper that the fraction collector was not started until after the first 5 ml of each run to avoid needlessly collecting the bulk of the void volume. Fractions from the fast protein liquid chromatography separation were assayed in each assay system usually after being diluted 50-fold with the appropriate dilution buffer to carry out the assay.

We remain confident that the evidence presented in our paper indicates a probable interference of rheumatoid factor in the Merck elastase assay, despite the criticisms levelled at our study by Drs Heubner and Utz of Merck and which we hope that we have replied to satisfactorily. Additionally, we find it very difficult to believe that the excellent correlation we obtained between rheumatoid factor levels and the discrepancy between our results and those obtained with the two assays are truly coincidental and that the same is true for the fast protein liquid chromatography data.

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