that a scientist who had worked in Gallo's laboratory, Mikulas Popovic, committed four "relatively minor" instances of misconduct by recording apparently false data from several AIDS experiments outlined in the 1984 papers.

Based on the findings, the ORI proposes that NIH — and any other federally funded institution that may subsequently employ Gallo or Popovic — monitor the scientists' "recording and reporting" of data for a period of three years. The ORI also recommends that NIH "consider whether any other actions are appropriate in relation to Dr. Gallo or the management of [his laboratory]."

Gallo and his attorney, Joseph Onek of the Washington, D.C., law firm Crowell & Moring, say they will appeal the ORI recommendations to the only remaining recourse, a judicial board within HHS.

But the Pasteur Institute's attorney, Michael A. Epstein of the New York City law firm Weil, Gotshal & Manges, claims the ORI report "is a significant event" in the renewed dispute over AIDS blood test royalties. Epstein has petitioned HHS to reopen the 1987 settlement that splits the royalties among Gallo, Montagnier, their institutions, and a foundation to fund AIDS research in developing countries (SN: 7/18/92, p.46). "This shows that the statements Gallo and the U.S. government made in 1986 to get the settlement were all lies," he asserts.

An NIH spokeswoman says the agency will await the outcome of Gallo's appeal before deciding upon taking any additional action against him. — *C. Ezzell*

Preventing AIDS pneumonia

(As the result of a production error, this article was difficult to read in the 1/2/93 issue. We regret any inconvenience this might have caused.)

Daily doses of the sulfa drug trimethoprim-sulfamethoxazole (TMP/SMX) help AIDS patients fend off recurrences of a life-threatening form of pneumonia more effectively than do monthly treatments with aerosolized pentamidine, according to a pair of studies comparing the two widely used preventive medications.

However, the authors of the studies conclude that because it produces fewer side effects than TMP/SMX, aerosolized pentamidine may still prove preferable for protecting some AIDS patients from *Pneumocystis carinii* pneumonia.

This form of pneumonia strikes many people with AIDS and kills a large number of them. In the mid-1980s, physicians began prescribing pentamidine or TMP/SMX — both of which are also used to treat established cases of *Pneumocystis carinii* pneumonia — for AIDS patients as a preventive measure. Without such therapy, 65 percent of patients taking the anti-AIDS drug zidovudine (AZT) who survive an initial episode of the pneumonia suffer further bouts.

In the first study, researchers led by Robert S. Holzman of New York University School of Medicine in New York City and W. David Hardy of the University of California, Los Angeles, found that 150 AIDS patients who inhaled an aerosol form of pentamidine once a month ran more than three times the risk of developing a recurrence of *Pneumocystis carinii* pneumonia as the same number of patients taking daily TMP/SMX. However, the researchers report in the Dec. 24 NEW ENGLAND JOURNAL OF MEDICINE, roughly one-fourth of the TMP/SMX patients had to stop taking the drug because it caused severe weakness or abdominal pain.

Researchers led by Margriet M.E. Schneider of the University Hospital Utrecht in the Netherlands report similar results in another study in the same journal. Schneider's team found that none of 142 AIDS patients taking daily TMP/SMX developed *Pneumocystis carinii* pneumonia, while six of 71 AIDS patients receiving pentamidine treatments monthly fell ill. — *C. Ezzell*

Cyclosporin-protein complex controls genes

Three research reports reveal new details of the molecular mechanism underlying cyclosporin's ability to prevent the rejection of transplanted organs and to slow fungal infections.

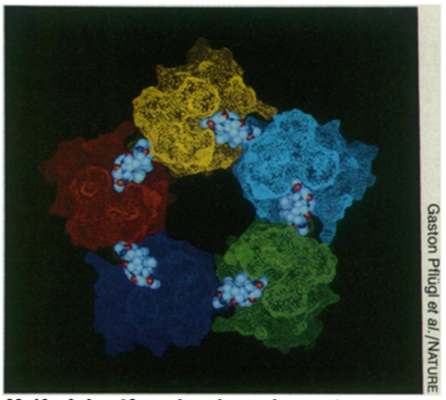
Cyclosporin works by first attaching to a protein called cyclophilin. This molecular duo then suppresses the responses of the immune system, most likely by interacting with an enzyme called calcineurin.

By pushing the limits of both nuclear magnetic resonance (NMR) spectroscopy and X-ray crystallography, two research groups have visualized this duo. Their separate reports appear in the Jan. 7 NATURE.

Earlier computer models had shown multiple connections between the two kinds of molecules. But some of these connections, called hydrogen bonds, were different in the real complex, says Stephen W. Fesik of Abbott Laboratories in Abbott Park, Ill.

Fesik and his colleagues used sophisticated NMR techniques to determine the structure of cyclosporin-cyclophilin pairs in solution. "The structures [obtained by the two groups] are remarkably similar," he says.

Unlike many other proteins, which twist or bend to make a tight fit with their partner molecules, cyclophilin maintains its shape when it binds to cyclosporin, adds Malcolm D. Walkinshaw, a crystallographer with Sandoz Pharma Ltd. in Basel, Switzerland.



Half of the 10-molecule cyclosporin (lightest blue)-cyclophilin (colored) complex.

Walkinshaw and his colleagues made crystals of this duo. But determining the exact positions of the atoms proved quite difficult. As they crystallize, these molecules congeal to form layered rosettes containing 10 to 12 pairs, he says. Thus, he could not study lone pairs, as did Fesik's group. However, while probably not the biologically active form, the rosette provides key information about each pair's structure, he adds.

In the crystals obtained by the Sandoz team, each of five cyclophilin molecules attaches to one side of each of five cyclosporin molecules. The shape of cyclophilin seems to promote the formation of a five-molecule unit, Walkinshaw explains.

To avoid contact with water, the five cyclosporin molecules then proceed to seek out five other cyclosporin molecules and to snuggle up against them. Thus, 10 cyclophilins wind up facing outward, with 10 cyclosporins sandwiched between them.

Each cyclosporin molecule arranges its amino acids into a ring with various chemical side groups sticking out. The crystal structure reveals that one hydroxyl side group in cyclosporin actually forms a hydrogen bond with its amino-acid backbone and not with cyclophilin.

This link helps maintain the shape of the cyclosporin molecule as it attaches to cyclophilin, says Walkinshaw. Researchers can now consider these details when they use computers to design new, possibly more effective surrogates for cyclosporin.

Using genetic engineering techniques, Thomas G. Larson and Donald J. Nuss of the Roche Institute of Molecular Biology in Nutley, N.J., have confirmed that this complex exerts its effects by altering the rate of gene expression. Cyclosporin ceases to work in chestnut blight fungus mutants lacking cyclophilin (SN: 8/8/92, p.84), they report in the Jan. 1 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES. — *E. Pennisi*