of BSC money which was being offered to the Gas Council would have proved a very mixed blessing and the BSC was unwilling to increase this figure. Although the price of between 4*d* and 5*d* a therm put forward by the BSC is comparable with that which ICI will be paying, the differences in structure between the two industries imply the need for very different criteria in costing gas supply.

One of the factors that must have swayed the Gas Council is that the ICI plants at Billingham and Severnside, which will be the main users of the natural gas, can be slotted tidily into the existing pipeline system of the gas industry, while the BSC's demand would have been more evenly spread throughout Britain. This would have required the construction of many new links, at considerable expense to the Gas Council. Furthermore, the ratio between the average and the maximum rates of delivery, known as the load factor, is likely to be considerably higher for the chemical industry than it would have been for the steel industry. This allows for a correspondingly more uniform and economical supply system. The Gas Council estimates that the gas industry's overall load factor will be increased by about 3 per cent as a result of the ICI deal.

The enormous size of the ICI contract can be seen from the fact that it has virtually doubled the sales of gas to British industry overnight. The 250 million cubic feet of North Sea gas that will be flowing into ICI plants each day will increase by about a fifth the total sales of the gas industry to its 13·5 million customers, and this represents more than the combined increase in total sales over the last two financial years.

Most of the natural gas will be used to synthesize ammonia at ICI's works at Billingham, Immingham and Severnside. This will replace more than a million tons of naphtha a year and will save an estimated £10 million a year in foreign exchange. The naphtha will also be freed for the production of other chemicals, such as methanol. The BSC's decision to rely on oil rather than raise its offer to the Gas Council shows that it is influenced by the flexibility which oil offers, as well as by a desire to avoid the large conversion costs needed to accommodate a new fuel. It may well be that the flirtation of the Gas Council with the two industries has produced benefit to all parties concerned.

DRUG COMBINATIONS

FDA in Earnest

AFTER stopping the sale in the United States of several dozen drugs which were either marketed by small companies or were of little commercial importance, the Food and Drug Administration of the US Department of Health, Education and Welfare has now decided to challenge three of the largest drug companies in the United States—Upjohn, Lederle and Squibb. On December 24, the FDA announced its intention of prohibiting the sale of twelve widely prescribed drug combinations, adding that any interested person who might be adversely affected by the decision had 30 days in which to submit evidence against the decision.

Like its previous decisions in this field, the FDA's proposal is based on the reports of a study group, set up by the National Academy of Sciences—National Research Council at the request of the FDA, which is reviewing the efficacy of nearly 4,000 drugs sold between 1938 and 1962. The twelve preparations which are likely to be banned are combinations of antibiotics or antifungal agents, and the point at issue is not whether the individual components are safe or effective but whether they are more effective in combination than alone. Seven of the twelve preparations—one a mixture of novobiocin and a sulphonamide, the other six various mixtures of tetracycline and novobiocin—are made by Upjohn. Four, mixtures of tetracycline and a fungicide amphotericin, are sold by Squibb and, completing the list, there is a mixture of tetracycline, hydrocortisone and phenylephrine sold by Lederle as a nasal anticongestant.

The drug companies maintain that the combinations are more convenient for doctor and patient alike than separately prescribed drugs and that combinations are more effective than the components alone. The study group and the FDA, however, have come to the conclusion that there is no proof of synergistic effects and they dismiss as hopelessly inadequate the tests, published in the medical literature, which purport to show synergism. One comment is that "a large number of papers purporting to demonstrate clinical efficacy of this combination were reviewed. No properly controlled studies were located, and most consisted of reports of a few patients treated with variable results. It is the considered judgment of the panel that this combination has no place in rational therapeutics and should not be marketed."

The reports point out that it is not simply that the combinations do not match the claims of efficacy made for them, but that they are hazardous as well. Needless exposure of patients to inessential antibiotics is bound to entail the risk that patients may be sensitized, while the same procedures may also assist drug resistant strains of pathogens. The antibiotic novobiocin, which is a component of six of the combinations under review, is singled out for special attention—it has a narrow antibacterial spectrum, it is one of three drugs against which micro-organisms readily develop resistance and it frequently induces adverse reactions in recipients. On these grounds alone it would be unwise to include it in a widely used combination drug. But the FDA also claims that the amount of novobiocin in the combination complained of is too low to be effective.

The FDA has much the same to say about the nasal suspension marketed as 'Achromysin'. This is a mixture of two decongestants, hydrocortisone and phenylephrine, together with the antibiotic tetracycline. The report says that "it seems unlikely that tetracycline in this form will effectively reach the organisms responsible for acute sinusitis, pharyngitis or other syndromes in which bacteria may be important pathogens" and the report seizes with some relish on the package insert which is said to contain the warning that "it may be inadvisable to augment local treatment by administration of tetracycline therapy in cases of infection".

The chances that the companies will be able successfully to appeal against the FDA's decision seem slim. It is difficult enough to pinpoint the effect of any one drug in a patient who is receiving several, without trying to prove that a combination is more effective than its components given separately. The ranks of academic medicine seem to be firmly behind the FDA on this issue.