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Resistance to Antimicrobial Agents

Response to the House of Lords Science and Technology Select Committee Inquiry

This submission was prepared by a group of Fellows chaired by Professor P.J. Lachmann Sec RS. The other members were Sir John Skehel, F.R.S. and Professor B.G. Spratt, F.R.S. It has been endorsed by the Council of the Royal Society.

We have considered the Committee's questions and offer the following comments.

We would like to stress the international nature of the issues under consideration and emphasise that effective solutions will not be achieved by the UK acting alone. Drug resistant organisms do not respect national boundaries and with the ease and rapidity of modern travel infections can be transported far from their origins very quickly.

The main reason for the current unsatisfactory situation is that, worldwide, there is no effective regulation of the use of antibiotics. In many nations drugs are freely available "over the counterî and even in countries where most drugs are only available on prescription there may be little control. The practice in some societies of doctors prescribing the most potent drug available - just in case - may be leading to resistance to drugs which for some infections are the final barrier before they become untreatable.

To try to remedy this situation before the complete arsenal of antibiotics is exhausted will require regulation, enforceable internationally. The regulation should include the following features:

- the availability of new drugs must be more effectively controlled than hitherto;
- the sale of drugs over the counter must be curtailed;
- the practice of prescribing the strongest drug without justification must be discouraged;
- the practice of not prescribing antibiotics for non-life threatening infections unless samples grown in culture are shown to respond to them should be encouraged;
- the introduction of any new classes of antibiotics, particularly those that are the sole effective treatment of infections, must be very carefully regulated.

We recognise the difficulty in implementing the above but there are already strains of enterococci and *Mycobacterium tuberculosis* that are resistant to all of the major classes of antibiotics and we believe that there is a likelihood that some strains of

additional pathogens may soon become untreatable. Thus the need for research and development of new drugs is urgent.

Drugs of several classes are required. If only one new class became available its likely overuse (in consequence of the lack of other effective treatments) would still leave open the prospect of resistance to it developing rapidly.

We recommend the vigorous encouragement of research to discover and develop new classes of antibiotics. In addition to natural product antibiotics we would encourage attempts to discover novel antibiotics, for example via development in combinatorial biosynthesis and synthetic chemistry. We would encourage research into the assessment of new targets for antimicrobial agents.

Development of effective vaccines for common childhood bacterial and viral infections would be particularly useful in reducing the worrying overuse of antibiotics in children.

Most of what we have said thus far pertains to bacterial disease. The problems with viral disease are due more to the dearth of effective chemical treatments than, as yet, to resistance, though there are some successful examples notably acyclovir against herpes. Vaccines have been developed against many viruses and the main hope for combatting such scourges as HIV also rests in the development of vaccines.

Similarly, the increasing chemoresistance observable in malaria infections, and the lack of any prospect of new antimalarials being available soon, suggest that the best hope for the future lies with developing suitable vaccines. Research in this area is also urgently needed as the disease is taking hold ever more strongly in areas where it had previously been easily treatable and, because of human migration and climate change, may continue to expand its range to embrace susceptible populations in areas that were not previously under threat.

However, the development of vaccines, especially live attenuated vaccines, has not been an attractive prospect for the pharmaceutical industry because of the possibility of insufficient return on the costs of development. The public both in the UK and elsewhere are, quite reasonably, averse to risk and as a result major trials of potential vaccines are required before they can be widely used. The development of resistance has reached such a serious stage that perhaps the question should now be asked whether the degree of risk that is deemed to be acceptable should be re-examined and safety-testing regimes simplified in order to allow products to reach the market faster.

We note that the terms of reference of the Inquiry do not include the use of antibiotics as growth promoters, and for prophylactic and therapeutic purposes, in animals and fish, nor the use of antibiotic resistant markers in genetically modified organisms, but welcome the fact that they are being considered by the relevant Government Advisory Committees.

Finally one important aspect of the development of bacterial disease resistant strains is the potentially very high cost of containment if they take hold in hospitals or other public institutions. Many of those resident in the UK will not recall the spectre of isolation hospitals for tuberculosis patients, but having to resurrect the concept on a large scale to deal with a resistant epidemic of TB (a situation that already exists elsewhere in the world) is not beyond the realms of possibility. Therefore, one further

recommendation we would make would be for the urgent development of a strategy to deal with patients infected with drug-resistant TB and untreatable vancomycin-resistant MRSA. This strategy will need to address difficult questions about confinement and monitoring of patients.