In 1928 Alexander Fleming discovered, more or less by coincidence, that penicillin was an effective treatment for bacterial infections. In the following years, the miraculous effectiveness of penicillin was further elucidated. When the Second World War required the US to send many troops to European battlefields, the US government made an appeal to local industry to produce penicillin in enough quantity to be able to treat wounded soldiers in the war. Pfizer responded to this appeal, and invested a large amount of money in developing a drug. The success of this investment made Pfizer the largest pharmaceutical company in the world.

In a way, the world has not changed that much. Since the 1990s it has faced the so-called microbial threat, caused by multi-drug resistant bacteria. Bacteria develop resistance—through Darwin’s principle of survival of the fittest—against antibiotics present in the environment. The World Health Organization (WHO) and health authorities all over the world have tried to reduce the risk these multi-resistant microorganisms pose. But if no antibiotics are available to treat infections, for example in a hospital, patients will die because they cannot get the surgical treatment they require. In the European Union, it is estimated that multidrug-resistant bacteria cause around 25,000 deaths per year. This number could go up dramatically if the pressure on existing therapies rises and no new antibiotics become available.

The challenge facing the world

The challenge the world faces is to prevent the enormous loss of healthy life that the spread of these multi-resistant bacteria could cause. There is broad agreement that a two-tiered approach is necessary to reduce the microbial threat. In the first place, initiatives are necessary to reduce ‘antibiotic pressure’ and limit resistance against antibiotics. The presence of antibiotics in the environment, often from misuse, is known as ‘antibiotic pressure.’ If the antibiotic pressure goes up, resistance develops. If it goes down, resistance is no longer an advantageous property, so it is lost. To achieve this reduction, professional guidelines aim at reducing the prescription of antibiotics if such treatment is not absolutely necessary. Antibiotics should not to be used in normal patient treatment; only in cases where no other treatment is available. A second important factor in respect to antibiotic pressure is to reduce the use of antimicrobial substances as growth promoters in agriculture.

In 1998 the WHO and the European Union raised the issue of the microbial threat at a meeting in Copenhagen. In 2001, recommendations from this meeting were transformed into an EU Council recommendation. It took until the 2009 Swedish EU presidency before a new political initiative was taken. Under the Swedish presidency, the EU Council adopted a resolution urging the European Commission and the EU member states to address the microbial threat. The Council commissioned the Commission to analyse possible solutions to the microbial threat. The problem also led to the creation of a transatlantic taskforce on antimicrobial resistance. All political attention is now directed on two issues: reduction of antibiotic pressure and the need for new antibiotics.

Most medicinal products are developed by pharmaceutical companies. Sometimes the initial research is done by government institutions, such as the National Institutes of Health in the US. But by and large, drugs are developed in anticipation of selling them on a market. To develop a new medicinal product an investment in the range of €0.5 billion is required. In exchange for providing capital for this activity, investors require a good return on their investment. Normally this has to be guaranteed in two ways: a solid protection of intellectual property rights and future sales.

The existing drivers and barriers to the development of a new medicinal product have been thoroughly analysed. Drivers can be summarized as a more or less safe return on the investment. Barriers include the risk of failure in the clinic and restrictive pricing and reimbursement after a product has been approved by a regulator.

A lot of valuable work has been done since the Copenhagen meeting. However none of the initiatives has thus far resulted in the launch of a new antimicrobial class. To achieve this goal – to get a new class of antibiotics into the hospital pharmacy – the current paradigm will not work. The focus on IP rights and market share is inhibiting progress. Therefore, a paradigm change is required. In future, investors should be earning a return on the basis of the innovative quality of the work achieved, rather than sales earned through inflated product prices. The market will not deliver the necessary new class of antibiotics. Instead, there will need to be some political intervention.

An approach that might work is global tendering. Governments would raise, or would guarantee, a certain amount of money for the development of a first-in-class antibiotic. They would call for tenders. Companies, or consortia, that win the tender would be awarded by the payment of a guaranteed flat fee. The fee would not be linked to the actual sales of a product or to its reimbursement from a contributing government. Rather, the reward would be linked to the product’s innovation.

The World Health Organization and political authorities around the world will need to accept that normal market mechanisms do not do the trick: the authorities will have to enter into contracts with the pharmaceutical and biotechnology industries to get these products produced. Governments will have to bear the development risks together with industry. Byshouldering some of the financial burden, governments will have the right to set research and development priorities in this very important area of medical need.

This article was written by John Lisman, an attorney and consultant at Lisman Legal Life Sciences in the Netherlands. Mr Lisman is also a member of the MedNous Editorial Board.