

Should public funding be invested in R&D for new antibiotics?

A statement from ReAct - Action on Antibiotic Resistance

The emerging problem of antibiotic resistance is a serious threat to global public health. There is a growing body of evidence showing that the situation is more severe than previously thought, with increasing prevalence of resistant and multi-resistant bacterial strains world-wide. It is also becoming clear that this is a multi-dimensional and very complex problem, the roots of which span over many different scientific areas and sectors of society. There will not be *one* magic bullet solution to resolve antibiotic resistance, but a variety of counter measures and actions targeting different aspects of the problem are needed.

Thus, the question is not whether or not we need new antibiotics – because we do – but by which mechanisms they should be developed to ensure that any new health technology or product is addressing a *global* need and that aspects of access and affordability are considered in the process. In addressing antibiotic resistance several areas need to be targeted:

- Improved rational use (which in principle equals more restrictive use both in human and non-human sectors)
- Improved infection control/hospital hygiene
- Development of novel antibiotics and complementary technologies (i.e. vaccines and new and/or improved diagnostic methods)

It is not a matter of either or – but each of the above areas needs careful analysis and focused effort.

Despite the magnitude of the resistance problem, little progress has been made in recent R&D for new antibacterial agents effective against resistant strains. The past thirty years have seen the emergence of only two new classes of antibiotics: oxazolidinones and cyclic lipopeptides, neither of which is effective against Gram-negative bacteria. The future for antibiotic drug development also appears bleak: among the top 15 pharmaceutical companies—which accounted for 93% of antibiotics placed on the market between 1980 and 2003—only 5 drugs in their R&D pipelines are antibacterials. This has two principal reasons: (i) the considerable scientific hurdles in identifying and developing new antibiotics suitable for human use and, (ii) an array of market-related factors that create weak or no financial incentives for pharmaceutical companies to engage in antibiotic R&D.

When stating that the public sector should consider supporting R&D for new antibiotics and related health technologies, this does not mean business as usual. A completely new business model is called for, where the value chain in drug development is re-engineered to harness the capacity of both the private and public sectors and to ensure that any forthcoming products are made available to those who need them in all parts of the world. Elements of such a new model could include for example:

- Open source platforms for knowledge sharing that create the opportunity for synergy among scientists across organizations and geographic barriers with common research interests.
- Shared compound libraries specific for antibiotic drug discovery. This would facilitate access to proprietary compounds for public-sector researchers, enhancing capacity for the development of new antibiotic agents. Creating such a library would help overcome the challenge presented by the Lipinski Rule of 5, which dictates the organization of many compound libraries and leads antibiotic candidates to be overlooked.
- Developing incentives for early development (crossing the “valley of death”) going from pre-clinical to clinical studies e.g. through Product Development Partnerships (PDPs)
- Support firms in low-income countries, small biotech, and scale-up of production at academic institutions that might enter antibiotic resistance R&D with lower opportunity costs and better economies of scale.

It should be noted however, that any public investment in drug development should be done in a framework of careful analysis looking at the different options to prioritize amongst health technologies and research goals to ensure greatest public benefit. Second, should new classes of antibiotics be discovered, measures must be taken to prolong their shelf-life through rational use and other potential mechanisms such as fixed dose combination.

Already today patients are dying because there are no existing antibiotics to treat multi-resistant bacterial infections. These highly resistant strains are not likely to disappear because of improved rational use alone.

In summary it is absolutely essential to avoid polarized stand points favoring *one* single option as the preferred solution as the problem of antibiotic resistance necessitates a broader approach in order to be managed. During the last year, there have been many developments in this area, notably by the EU-US Task Force, IDSA, BSAC, RFF, APUA, ReAct, and a number of other initiatives and we cannot afford to miss the opportunity. We are facing a global problem that requires joint action by all concerned actors.