Answer key, study questions part 3

1. For Gram negative bacteria. Resistance rates to currently available antibiotics targeting Gram negatives are particularly high. Generally speaking, development of new antibiotics is scientifically demanding, but particularly so for Gram negatives since they have two cell membranes. It is difficult to find non-toxic antibiotics that are able to penetrate the outer as well as the inner cell membrane. Hence, the set-up of currently available (and effective) antibiotics for Gram negative bacteria is limited.

2. Antibiotics are divided into different classes based on their chemical structure. Antibiotics of the same class generally have a similar mechanism of action. Thus, bacteria resistant to a particular substance in a particular antibiotic class is often also resistant to other members of the class. This is referred to as cross-resistance.

3. The resistance problem can never be fixed, only managed. As a consequence of bacterial evolution and natural selection, resistance will at some point emerge to any newly developed antibiotic substance. It will be evolutionarily advantageous for bacteria to be able to curb the effects of harmful substances (i.e. antibiotics) upon exposure, since they otherwise will die off or be hindered from growing and proliferating. Hence, in the presence of antibiotics, antibiotic resistance will be selected and we will therefore have a continuous need for influx of new drugs with alternative mechanisms of actions.

4. Some of the alternative treatment strategies mentioned, like phage therapy, will only target very specific types or subtypes of bacteria (for example particular strains of a bacterial species). This will exclude them as alternative treatments for severe and life-threating infections that require immediate attention and cannot await laboratory diagnostic results (besides, we currently lack good, rapid, affordable diagnostic tools that can aid in making such, and simpler, clinical decisions). I.e., for susceptible bacteria that are treated empirically, the risk of treatment failure increases as the spectrum of antibiotic activity becomes narrower.

5. Bacteriophages are viruses that target bacteria. Upon entering the host cell, they can start to proliferate and produce more viral particles which eventually will cause the bacterial cell to burst. This procedure is undertaken by so called **lytic** bacteriophages or, alternatively, by **lysogenic** bacteriophages that have entered the lytic phase of their life cycle.

6. Universal access to vaccination would decrease the incidence of (particular) infectious diseases, which in turn would lower the need for antibiotics. This applies also for vaccination against viral diseases, since

health-care visits and incorrect use of antibiotics expectedly would decrease along with a lowered incidence of certain viral infections. Besides, the incidence of secondary bacterial infections (for example bacterial pneumonia following influenza episodes) would decrease as well.

7. Ideally, new business models would decrease the economic risks of companies that currently are tightly connected to (the lack of) antibiotic innovation. As of now, we are asking companies to invest money in developing products that ideally should be sold as little as possible, which of course is economically unattractive. Introduction of new business models, in which the economic risks are shared among stakeholders, could potentially stimulate antibiotic innovation while at the same time decreasing reliance on high volume sales and high prices of new products.

8. In the context of antibiotic innovation, de-linkage means separating the cost of investment for companies from the product price and the sales volumes. This is important since reliance on high prices of new antibiotics would have a negative impact on global access to antibiotics. I.e. high prices would hinder poor people from receiving antibiotic treatment when needed. Besides, reliance on high volume sales would negatively impact conservation of antibiotics (i.e. correct antibiotics use and antibiotic stewardship).

9. A public-private partnership is a collaboration between stakeholders from different sectors that aim to jointly work on, and/or take economic responsibility, for antibiotic innovation. For example, tax money could be used to reduce the economic risk of companies to focus on antibiotic innovation and scientists from public universities could be brought into collaborative antibiotic innovation projects together with pharmaceutical industries.

10. The access/excess dilemma refers to the difficulty of ensuring access to antibiotics to all in need while at the same time reducing excessive use of antibiotics which drives antibiotic resistance development.