BSL: Better Safe than Lucky?

Last April, public health agencies including the World Health Organization (WHO) and the US Center for Disease Control and Prevention (CDC) instructed 4,400 laboratories worldwide to destroy virus samples from a proficiency kit, which they had received to evaluate their diagnostic abilities. The problematic sample was the strain of influenza known as H2N2 that caused the devastating flu pandemic of 1957–1958. With the recent surge in research activity on dangerous pathogens—a result of disease emergence and of the emphasis on bioterrorism threats—the risk of such incidents is growing, and scientists and their regulatory agencies are under increased scrutiny for their ability to contain dangerous agents. The challenge will be to take measures to prevent such major safety glitches without impeding research and diagnostic activities.

In the scientific community, reactions to the H2N2 incident have been mixed. Some call the story overblown, arguing there were no adverse consequences; others consider that we just were very lucky this time. The fact is, sending the influenza H2N2 strain to unsuspecting labs has exposed laboratory workers to an unnecessary risk. Because the strain has stopped circulating among humans since 1968, anybody born after this date has no immunity against it and upon infection risks serious illness or even death.

The decision to include H2N2 in the proficiency panel at the US-based manufacturing company was a serious error of judgment. Its implementation was possible because nothing in the US biosafety regulations set H2N2 apart from other influenza strains. In some other countries such as Canada, however, H2N2 was flagged as belonging to a higher risk group. How is such a discrepancy possible? Is there no international classification of infectious agents in risk groups?

The short answer is no. This classification is established by national authorities in line with WHO guidelines. Although it may seem odd at first, assigning risk groups on a regional basis makes sense. There are local factors that affect the risk posed by an infectious agent, such as its mode of transmission, the level of immunity in the local population, and the local availability of preventive measures and efficient treatments.

The WHO, however, provides the definition of four biosafety levels (BSL) describing safety elements of the facilities, special practices and protective equipment. The BSL for a given pathogen is only partly dictated by its risk group. In the United States, the CDC, in collaboration with the National Insitutes of Health and ad hoc experts, drafts recommendations of which BSL should be used for specific agents and publishes them in a manual (http://www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4toc.htm). These recommendations are only advisory and are intended as a basis for risk assessment in individual laboratories, depending on the nature of the work. Regulations are then established locally by institutional biosafety committees.

CDC only has regulatory authority over a list of 40 'select agents' established in the context of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002. What is at stake for these agents is not biosafety but biosecurity —the prevention of their intentional misuse or diversion. In the United States, biosecurity measures include laboratory registration, government approval of personnel, preapprovals of shipments and extensive reporting.

After the H2N2 incident, CDC has announced that it will reevaluate whether to add certain strains of influenza to the select agents list. But the reason why no influenza strains were included originally was a legitimate concern that the additional security measures may impair the quick response to an emerging pandemic strain—a concern that still applies.

Instead of adding pathogens to the select agents list, in most cases, it would be more effective to provide better guidance for risk assessment. As far as biosafety is concerned, on paper, the principle of risk assessment is a sensible solution to promote adapted safety measures without impeding research. In practice, however, it requires appropriate, detailed guidance.

In some cases, such as for HIV, the guidance is detailed and works well: there is a range of recommended safety measures depending on the type of experiments. In the case of influenza, the recommendations were not as explicit and clearly needed revamping. CDC has now also announced their pending revision in the upcoming edition of its manual, and has published a draft version on its website as interim measure. The application of these updated, more detailed, recommendations should be sufficient to prevent the repetition of the H2N2 incident and similar events.

Without confounding biosafety and biosecurity, it is crucial to improve the framework for the valuable risk assessment principle to work in practice and to provide assurances to lab workers and the community that they rely on appropriate safety measures, not just on luck.