

BIOBUSINESS BRIEFS

MARKET WATCH

Landscape for medical countermeasure development

Medical countermeasures (MCMs) encompass biologics, drugs or devices that may be used for biodefence against biological, chemical or radiological bioweapons, or in the event of naturally occurring emerging and re-emerging diseases, or natural disasters. Since 2008, the Tufts Center for the Study of Drug Development (CSDD) has routinely explored the R&D landscape for MCMs. Here, we present the findings of CSDD's most recent review, completed in 2016.

The most substantial change in the landscape in the time-frame of the CSDD analyses is the size of the MCM pipeline. In 2008, we identified 263 MCMs in development; by 2016, the number of MCMs in the pipeline grew to 592 (FIG. 1a). Similar growth has been observed in the number of companies in the field, with 133 companies identified as working on MCMs in 2008 and 303 companies in 2016. Broadly speaking, companies in the MCM field are typically privately owned, small to medium-sized enterprises (SMEs), with a biotechnology focus. Although more than half of these companies (159; 52%) have their headquarters in the United States, the proportion of non-US companies has grown since 2008. China, with 33 companies, the United Kingdom, with 12, and Canada

and Switzerland, both with 10 companies, complete the top five countries engaged in the field.

Continued, steady pipeline growth seems to indicate a positive impact from programmes intended to encourage and support the development of MCMs, such as Project BioShield in the United States, which was established in 2004 with an initial budget of US\$5.6 billion through fiscal year 2013, and has been managed by the Biomedical Advanced Research and Development Authority (BARDA) since 2006. BARDA and Project BioShield budgets have grown steadily, with increases in 2016 totalling more than \$400 million over their 2015 budgets. Much of the support comes in the form of Broad Agency Announcements and Funding Opportunity Announcements, which allow smaller companies to compete for grants, awards and contracts by conducting specified research projects.

This support for SMEs is vital as they are developing 86% of all MCM products in the pipeline. Looking at the numbers differently is also telling. Of 2,310 total products in development by the top 25 biopharma companies, only ~3% are MCMs, whereas MCMs comprise a mean of 27% of the portfolios of SMEs involved in the MCM field.

Another aspect of the MCM landscape worth examining is the relative role played by large biopharma companies and SMEs in moving products from early development to later stages. Of the 592 products in development, 488 (82%) are at early stages (phase I or earlier). However, among the MCMs being developed by large companies, only 65% are in early development, whereas among SMEs that figure rises to 86%. So, large companies are important for getting products through later-stage development to market, but the seedbed for discovery to early development is in SMEs.

The five most prevalent indications in the MCM pipeline (FIG. 1a) provide some insight into a strong driving factor for the companies' choices of MCM indication — all five of the most common MCM indications have applications other than biodefence. Influenza MCMs are by far the most prevalent: there are 125 universal vaccines or vaccines for potential pandemic threats in development, which alone make up 21% of the MCM pipeline (FIG. 1a). A broader look at all influenza products in development shows rapid growth from 103 products in 2008, to 314 in 2012, to 537 in 2016 (FIG. 1b). Frequent influenza outbreaks make this rapid and sustained growth in the pipeline unsurprising.

Similar, although less dramatic, trends can be seen among other top MCMs for which there have also been recent outbreaks. In 2014, there was the largest outbreak of Ebola in its 40-year history, and the number of Ebola MCMs increased from 9 in 2008, to 30 in 2012, to 76 in 2016 (FIG. 1b). Similarly in 2015–16, there was the first large outbreak

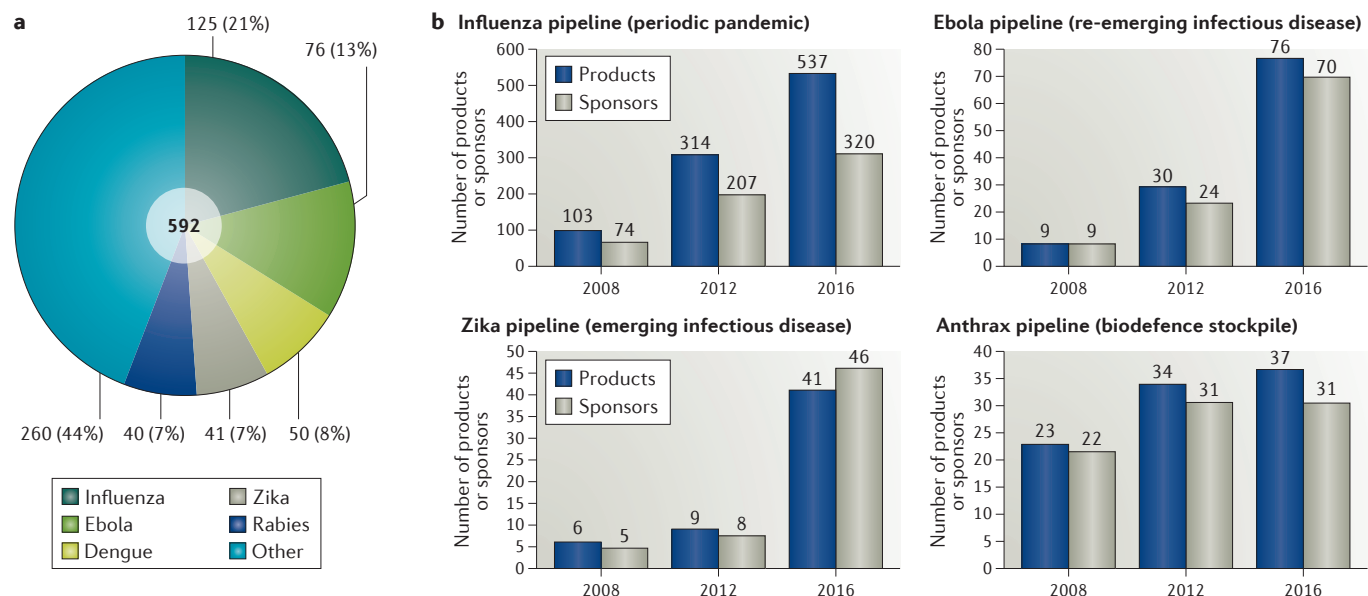


Figure 1 | **The pipeline for medical countermeasures.** **a** | Number of products in development for the five most common medical countermeasure-related indications. **b** | Trends in the pipelines for selected medical countermeasures, illustrating the different drivers of product development.

of Zika, and MCMs increased from 6 in 2008, to 9 in 2012, to 41 in 2016 (FIG. 1b). These events demonstrated the urgent and unmet medical needs for treatment and prevention presented by emerging and re-emerging infectious diseases that are naturally occurring, sporadic and non-biodefence, yet potentially profitable, as future outbreaks of these or similar diseases are very likely. On the other hand, biodefence-only countermeasures tend to be purchased in bulk by governments, and placed in readiness in something like the US government's Strategic National Stockpile. Ideally such MCMs are rarely or never used, eventually reaching a target plateau in terms of 'market' growth determined by the requirement to replace expired stock or expansion in the populations at risk. *Bacillus anthracis* infection illustrates this point well: in 2008 there were 23 countermeasures being

developed, in 2012 there were 34 and by 2016 that number had essentially plateaued at 37 (FIG. 1b).

Given that more than half of all MCMs in development (332 products; 56%) are for just five indications (FIG. 1a), it is clear that industry efforts are concentrated on a relatively narrow subset of the potential threats. The remaining 57 indications on the US National Institute of Allergy and Infectious Diseases (NIAID) list of emerging infectious diseases and pathogens have a total of only 289 products currently in the pipeline, averaging 4.5 MCMs per indication (ranging from 0 to 37 per indication). Some very deadly diseases are in this group. Marburg virus, a virus related to Ebola, currently has only 12 MCMs in development, 9 of which are still in discovery. Eastern equine encephalitis, for which there are small but recurring outbreaks in the United States,

is the deadliest mosquito-borne disease in North America, but has only four MCMs in development.

Overall, it seems that while the budgets and prioritization schemes of government departments such as NIAID and BARDA affect the overall size of the MCM pipeline, it is current and recent world events — particularly emerging and re-emerging disease outbreaks — that determine which MCMs have pulses in pipeline growth.

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