

Biocontainment in Low Income Countries: A Short Discussion

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Introduction

The keys to combat infectious diseases in developed countries are out there. And “there” are the low and medium income countries where the most of these emerging and reemerging diseases are hitting and threatening public health. One of the tools in this fight is biocontainment facilities, to perform safe research on these pathogens. The approaches to biosafety and biocontainment facilities is diverse: in our opinion, modular BSL3 facilities, already tested in manufacturing premises, instead bigger or site by site infrastructures, could be set up in such countries to process samples “on site” giving, ideally, better surveillance, short times to obtain results, and an increase in human capabilities and life-long education, and job opportunities, for scientists and technical staffs in that countries.

In the last decades, sharply in the last years, emerging and reemerging diseases, most of them zoonotic, have come up on the floor. New infectious diseases have been emerging at the unprecedented rate of about one a year for the past decades, a trend that is expected to continue [1]. SARS coronavirus [2], several highly pathogenic strains of avian influenza virus [3,4] new H1N1 influenza, MERS coronavirus [5], Ebola, now virus Zika [6], and no one have idea which will be the following. Unknown or poorly known diseases are hitting old areas or making broader its spreading areas, sometimes on the ride of human trade, or global warming, or infestation of naïve areas by arthropod vectors.

In parallel, this increased concern, mixed with some drops of bioterrorism’s threats, has fueled the design, construction and operation of a plethora of new biosafety-biocontainment facilities and/or laboratories the most of them in developed countries [7,8], where these emerging diseases are only seen if they are carried in by tourists or migrants. As pointed out for BPP [9], at least thirty-four operational BSL-4 laboratories in twelve out of the nineteen countries surveyed were detected, and only five of them allocated in low, medium or emerging countries.

A non-profit organization specializing in security matters estimated in 2011 that roughly 40 BSL-4 labs existed or were under construction worldwide [10], although some researchers consider that an overestimate [8]. The number of U.S. BSL-3 labs registered with the United States Centers for Disease Control and Preventions’ Select Agent Program increased from 415 in 2004 to 1495 in 2010 [7], but the actual number of BSL3 facilities is higher; at 2011 the number of UK organizations which manage BSL-3 facilities reached around 350 owning 600 sites at 2011 [11].

There are, of course, dozens of dozens but not several hundreds of biocontainment facilities designed, set up and actually run in low and medium income countries, and in emerging countries, in the areas where pathogens and vectors are “normal” components of the

ecosystem (Bangladesh, India, Indonesia, China, Brazil, and Mexico among others). These BSL3 facilities are giving services to more than 2/3 of human population on Earth, in areas where epidemiologic modeling suggest than a global influenza pandemic could cause more than 90% of the global human deaths, mainly in Sub-Saharan Africa and South Asia [12]. Although the economy of some of such countries could not afford them, if a real governmental commitment is not achieved, there are lot of reasons (development of industrial and service suppliers, education of local microbiologist/virologist on site, promoting development of new surveillance nets) to encourage a developing country to commit on it, indeed through international research collaborations [13].

High Biosafety Facilities Concepts

The construction of BSL-3 or -4 facilities is highly technical, and there few universally recognized standards. The improvement of laboratory capabilities requires investment in both time and money [14]. Any wrong (or non-right) decision could have significant cost repercussions. Indeed small laboratories have high costs; the total construction cost of around 30 m² lab and equipment investment, at 2009, accounted 400.000 US dollars [15]. Start-up consumables and reagents for one year cost additional US\$ 134,655. We must also consider that building costs for a BSL-3 facility typically exceed those of a BSL-2 by 200-400%, and this difference becomes larger when operational costs come into play (from 200-800%) [16]. It has been estimated that the annual maintenance budget for high containment laboratories is often 10%-15% of the facility construction cost [17]. Comparatively the costs (around US\$ 200.000) and lead times (12 weeks) and container maintenance (annual certification and every 5 year repainting) seem clearly less expensive [18]. Quite often, the initial budget is spent on infrastructure and equipment without considering the required costs of further operation and facility maintenance, or the training and updating cost for technical staff. In other words, obtaining money for new labs can be much easier than finding money for long term maintenance of the old ones. So, today’s decision must be kept firmly for decades if we want actually obtain fruits of such decision; it is essential that long term goals are set and that the finances are made available to enable and sustain continuous quality improvements [14].

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The Size Could be Important

But it is not necessary to build a very large and cutting edge state-of-the-art high biosafety laboratory (with high initial cost and higher maintenance costs) if you simply have troubles to assure proper supply of electricity or you have not knowledgeable staff to run it.

Although high technified and complicated facilities are the general rule in developed countries, there are, also, offered by several companies, small modular systems which allow set up a BSL3 facility once the main supplies (power, water, and diesel) have been secured. This solution, shipping containers, manufactured by Certekinc, Germfree, Getinge Group, HMK Bilcon, KF Mobile Systems, Labover, among others, acting as small biocontainment boxes, with long history of being converted into offices, homes, and for other uses [18], has been previously suggested by experts for particular pathogens endemic regions, presenting a lower biosecurity risk than in developed countries [19]. The ZAMSTAR TB Prevalence Survey (2009-2011) relies, among other facilities, in a containerized BSL3 TB laboratories (CTL) designed and built for such purpose. The BSL3 modular systems, negative pressure boxes at the end [18], are enough flexible to be adapted to specific requirements and are extremely robust, and a perfect weather-proof superstructure within which a laboratory can be constructed [18]. And allow, with some arrangements, future increases of BSL3 areas by deploying multiple containers alongside one another or be interconnecting modules [18]. This is not, however, a general opinion, as others have considered building structure instead of buying a modular laboratory because modular design may not be easy to sustain and durable given the challenges in terms of environment, electricity instability, and lack of technical expertise in case of system breakdown [15]. Nevertheless, it should be warned that architectural and engineering consultants, who typically receive a percentage of any specific facility's construction cost, have a strong incentive to over design, which can increase both upfront and maintenance costs [11] in the building process. Modular container laboratories (MCL) can reduce the price of an installation by 2- to 3-fold with respect to traditional brick and mortar construction [18]. The CTL and its successor, the MCL, have been spread in the last years; there are now 15 CTL/MCL in 7 countries in Africa, South America and the Caribbean.

Another strategy is to purchase BSL3 laboratories as a pre-finished casework, made of non-corrosive water tight material, ready for installation [20]. At destination, such pre-finished casework is completed with a ceiling, a floor and provisions for creating necessary openings, using measurements of the actual room into which it will be installed. All interior surfaces are therefore easy to clean and resistant to corrosion by disinfection and decontamination procedures. Upon installation, power and air conditioning lines and systems are drilled into the walls or ceiling and any cracks or gaps sealed airtight. However, as far as we know this approach can lead to increase maintenance costs as at the end we are dealing with a new structure inside an old structure also requiring supervision and maintenance.

As these aforementioned modular systems (currently shipping containers) have been tested previously to be shipped by the companies and they have an historical of previous manufacturing and commissioning, the systematic checks of compliance to specifications (critical containment points such as joints and penetrations, electrical system, access control, air filtration, waste treatment devices, etc.) and validation performances to be carried out in site are easier and faster than for "concrete" buildings [18]. This validation will give us a realistic picture of the capabilities of the bio containment facility in site, according to specific protocols already tested in the factory.

Moreover, the shipping containers can take advantage of previous energy saving features checked in former models or approaches, reducing maintenance costs [21]. Modular shipping container systems, however, as scientific equipment without going any further, should have an expected working lifespan clearly exceeding 10 to 15 years, if not frequently moved surpassing the lifespan of low and medium-quality conventional brick and mortar building [18], with enough spares availability in the long term and firmly avoid suspicions of planned obsolescence; this may be quite crippling to low and medium income countries where funding and importation are major difficulties [22].

Not every laboratory, and this is clear in small BSL3 modules, should be expected to deliver every possible service, and integration into regional and broader international networks should be a part of the overall strategy. This strategy and the exchange of experiences, procedures, troubleshooting and its solutions, and personnel should be easier if facilities share similar constrains and approaches as it is the case of the modular systems.

It is possible that a double standard system will be generated depending on the geographic area, also driven by budget differences. As pointed by Heckert [17] it should rely less on cutting-edge, modern safety equipment to reduce risk and instead combine a thorough risk assessment with procedural modifications to reduce the weight and amount of more technical and power demanding devices. This was also pointed out for TB laboratory capacities in resource limited settings [23] in order to avoid over-engineering for the actual biosafety risks encountered. This double standard, in itself, is not a bad approach provided that the worker's safety remains at the same level in both standards. In other words, laboratories equally safe for the people inside but with different safety threshold (containment, barriers) outwards.

In any case, and applying the same acronym used for a generic framework for safer, more secure, and sustainable laboratory capacity building [24], a BSL-3 in all countries but particularly in low and medium income countries has to be; Sustainable: laboratory operation can be maintained independently over a long-term period; Affordable: the facility should not depend on external aid for core functionality; Functional: the laboratory staff are safer than currently through live long education and active training in the same facility; there is less risk of the laboratory being the source of the infection and the presence of new surveillance and diagnostic capability keeps the community safer; Effective: laboratory is devoted to the most suitable research application or diagnostic activities for such specific environment or region and Realistic: laboratory facility is an answer to questions or services that the country or the region, actually has. So, SAFER arises, for people but also for the budget of the country.

There is no "one size fits all" approach and we must continue to be open-minded and flexible in our thoughts [25]. Coping with the lack of reliable 24/7 infrastructure services such as water and power and limited funding, an efficiently basic and small laboratory leads with creativity, resourcefulness, can subsequently being able to safely conduct vital work. These on-site scenarios, taken together with modern but plain "Western-style" approaches, as could be basic module systems (similar and exchangeable) can result in a balanced solution that may have wider applicability on a global scale.

Final Remarks

Although the strength of a chain is based on its weakest link [19], we all have to persist in this devolution of capabilities of BSL3 pathogens surveillance, diagnostic and experimentation to such

countries through research consortia, scientific collaboration or rooted partnerships all of them requesting long term investment and planning, even when wealthy countries face no immediate outbreaks threats [26] arising in low and medium income countries. We should remember that, in most cases, the release of the pathogen in such countries, still unfortunately, will not imply nothing more than an additional input to the normal circulation of such pathogen in the wild. We have to protect the workers at the same levels and use equivalent protocols and personal protective equipment than developed countries workers but the bio risk for the environment is definitively lower.

But this, this is another history.

Conflict of Interest Statement

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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