Emerging zoonoses and biocontainment: a necessary but complicated relationship

Xavier Abad

Head of the High Biocontainment Unit of IRTA-CReSA CReSA Building. Campus Universitat Autònoma de Barcelona. Cerdanyola del Vallés. Barcelona.

Enf Emerg 2026;25(2):62-66
doi: 10.18176/enfemerg.0015

Summary

High and Maximum Biocontainment facilities, what we call BSL3 and BSL4, respectively, are an essential tool for working with biological agents (usually viral in nature) that cause emerging or re-emerging infections. In the last two decades, their number has increased dramatically, and since the advent of COVID19 this pace has accelerated worldwide, despite the social context not very favorable to them. These facilities, the leitmotifs of which must be Biocontainment and Biosafety, are a technological challenge in their design and construction and an economic challenge in their construction and further maintenance. And as Biosafety is also a process, it requires technically qualified and trained personnel, and active on a continuous basis, which also has a not negligible cost. Surprisingly, there are no international standards regarding the construction of these facilities, and the subsequent management of biological risk, only a framework of guides and recommendations, and some ISO standards that are not mandatory either. These facilities must be used continuously for their own activities but must also be opened, reasonably, to external users/researchers maintaining a difficult balance between biosafety and biosecurity. Making them safe or safer while being more efficient and sustainable is the wine that is in the Safe Grail that everyone is looking for.

Keywords:
Biocontainment. Biosafety. Biological risk, Standards. Open Access facilities. Emergent zoonoses.

Zoonosis emergentes y biocontención: una relación complicada pero necesaria

Resumen

Las instalaciones de Alta y Máxima Biocontención, lo que llamamos NBS3 y NBS4, respectivamente, son una herramienta imprescindible para el trabajo con agentes biológicos (normalmente de naturaleza vírica) que causan infecciones emergentes o re-emergentes. En las últimas dos décadas su número se ha incrementado espectacularmente, y desde el advenimiento de la COVID19 este ritmo ha acelerado en todo el mundo, a pesar del contexto social no muy favorable a las mismas. Estas instalaciones, cuyos leitmotivs deben ser la Biocontención y la Bioseguridad son un desafío tecnológico en su diseño y construcción y un desafío económico en su construcción y mantenimiento. Y como la Bioseguridad es también un proceso, requiere de personal técnicamente cualificado y formado, y activo de forma continuada, que también tiene un coste nada despreciable. Sorprendentemente no existen estándares internacionales en cuanto a la construcción de estas instalaciones, y la gestión del riesgo biológico posterior, sino un entorno de guías y recomendaciones, y algunas normas ISO que tampoco son obligatorias. Estas instalaciones deben utilizarse de forma continuada para las actividades propias, pero deben abrirse también, razonablemente, a usuarios/investigadores externos manteniendo un difícil equilibrio entre bioseguridad y bioprotección. Hacerlas tanto o más seguras y al mismo tiempo ser más eficientes y sostenibles es el vino que se encuentra en el Grial Seguro que todo el mundo busca.

Palabras clave:
Biocontención. Bioseguridad. Riesgo biológico, Estándares. Instalaciones de acceso abierto. Zoonosis emergentes.

Correspondencia: Xavier Abad
E-mail: xavier.abad@irta.cat

Introduction

In the first two decades of the 21st century, several global threats to public and animal health, such as highly pathogenic avian influenza (since 1997), SARSCoV1 (2002-2004), African swine fever virus and classical swine fever virus (always present in many countries), MERSCoV (since 2012), Ebola in Zaire (2014-2016 epidemic and many subsequent aftershocks), Marburg (2004-2005, Angola and more) have emerged or reemerged periodically. As can be seen, with a high representation of zoonoses (they represent 60% of emerging infectious diseases and 72% of those have their origin in wildlife[1]). At the same time, the number of biocontainment facilities experienced a sustained and arithmetic increase. In the American case, with the bait of the anthrax attacks of 2001[2], but the phenomenon was global[3].

But it is since the appearance of COVID-19 caused by SARSCoV2 that the number of High and Maximum Biocontainment facilities, which responded differently depending on the regions or their capacities[4], or the plans to build them (which is not the same) has not stopped growing, almost geometrically, both in terms of projects and in terms of execution. Because this is also an important issue, between the desire to execute a design that generates a basic project and the start-up of these facilities the minimum period exceeds five years, if all the factors align favorably. And they usually do not align. In the opposite sense, COVID-19 has generated a kind of hypersensitivity in certain social groups that, for each new health emergency, generates intense responses against certain public health measures and the presence or new construction of this type of facilities.

The current scenario is that there have been a few more than 10 BSL4 facilities at the beginning of the 21st century to more than 60 facilities operating or under construction this 2026[3]. The number of improved BSL3 facilities (abbreviated as BSL3+, a "+" that can accommodate conceptually different, not very comparable facilities) is also clearly much above 60, with a more moderate increase. An initiative that lists some of such facilities, with obvious shortcomings for those who know this field, but nevertheless useful, can be found at the following link, https://www.globalbiolabs.org/map.

This article briefly discusses the current expansion of high- and maximum-biocontainment facilities, with particular attention to the Iberian context, their costs, operational challenges, sustainability, and the need for harmonized standards.

High biocontainment in the Iberian Peninsula

There are dozens of BSL3 facilities in the peninsula, many of them small sized. Muluneh *et al.*[5] estimates these facilities at 12, three times less than those available in Sweden, and 7 times less than those counted in Germany. These numbers might seem contradictory, but they depend a lot on the inclusion criteria; all BSL3 laboratories regardless of their size, large BSL3 facilities, BSL3+ facilities, BSL3 facilities for large animals (also labeled as ABSL3-Ag), private production facilities and more. Large facilities, which follow the Sandwich model, with three plants inside Biocontainment, the system that provides the most protection or safety, can be counted on the fingers of one hand.

Two of them, CSIC-CISA-INIA and IRTA-CReSA, constitute the RLASB, *Red de Laboratorios de Alta Seguridad Biológica*, which has Open Access for the execution of studies that require high Biocontainment, at cost price.

Maximum biocontainment in the Iberian Peninsula

Until 2026 there was no actual Maximum Biocontainment unit in the Iberian Peninsula. Now there is a private one, managed by the company Glaxo Smith Kline, which operates on its own projects and a design with class 3 cabins, not suite type. The class 3 cabin model is historically the usual one in Great Britain, but has had very little success in continental Europe, which leans towards the suite type. And in an undetermined period, not before 2029, there will be two new BSL4 facilities, both located in Madrid, one managed by ISCIII and the other by CSIC-CISA-INIA. If these planned facilities become operational, Spain would substantially increase its maximum-biocontainment capacity within the European context. The definitive history of the ISCIII BSL4 facility begins in 2021, with the announcement of its project and construction management tender[6] and the Memorandum[7]. Regarding the BSL4 facility to be located in Valdeolmos, managed by CSIC-CISA-INIA, the political decision (with a significant prior definition work) was taken in 2025[8].

Wills and costs, a burden

If we assume that emerging and re-emerging infections, not necessarily zoonotic, will be a constant in the coming decades, as they have been in recent decades[1] the need for these facilities to experiment with new vaccines and treatments, but also to understand the mechanisms of infection, pathogenesis in ecological hosts or in potential new hosts, or in animal models, is obvious. For example, no one thought that the highly pathogenic avian influenza virus H5N1 would jump to cows; when it did, it was necessary to experimentally know the internal dissemination, pathogenesis, excretion in this new host. Without a High Biocontainment facility (at least) this would not be possible[9]. But the will must be ironclad over time; to cover the design and construction, to fight against an unfavourable social perception (especially after the outbreak of the COVID-19 pandemic, and the very poorly managed doubts about its origin), and to cover the maintenance and updating of these technological facilities, the always forgotten issue by governments and universities of all conditions.

Currently, a BSL3 laboratory can cost between 10,000 and 15,000 euros per square meter to build, depending on the location and specific requirements (own data). While these costs are substantial, they are generally manageable for institutions such as universities or regional health departments. Several factors, such as local labor costs, material availability, and regulatory requirements, can influence the final budget.

BSL4 facilities incur significantly higher costs, approximately double, at 27,000 euros per square meter (Table 1). The high cost of BSL4 construction is primarily attributed to the need for advanced containment measures, robust HVAC systems, and the integration of specialized decontamination equipment into the facility. In the absence of clear and harmonized standards, the cost of some BSL3 facilities may approach that of BSL4 laboratories, depending on the engineering solutions and containment systems selected. Therefore, no one is preventing the cost of a BSL3 from rising to 25,000 euros, depending on budget availability, but what is clear is that a BSL4 cannot cost (in countries like ours) less than 25,000 euros per square meter.

BSL3 facilities, although energy intensive, have relatively lower operational demands. The systems are less complicated, the equipment is not as specialized, and the training and certification of personnel is not as rigorous or frequent as in BSL4 environments. The annual operating cost is approximately 800-900 euros per square meter. In comparison, BSL4 laboratories show exponentially higher operational costs, again double, at around 1,800 euros per square meter (Table 1). Other calculations point to annual maintenance costs in BSL3 between 5 and 8% of the initial equivalent construction costs[10]. And for Maximum Biocontainment (BSL4) we would reach 10%[11].

Table 1. Average cost (in euros) of BSL3 or BSL4 facilities.

	Construction costs (euros per m²)	Operating costs (euros per m²)	Maintenance cost (%)*
BSL3	10-15,000	900	5-8%
BSL4	27,000	1800	10%

*(%): percentage of construction costs.

These costs can be prohibitive. In fact, there are several facilities in Spain and Catalonia that were built as BSL3 but are operating as BSL2, and sometimes not in a regular basis but sporadically, with the economic inefficiency and loss of scientific capacity that this entails. In these cases, the diagnostic need and research must generate the instrument, if we want it to be sustainable. And in countries outside the first world the approach must be different[12], based more on risk assessment as a pillar than strictly high design, or expensive engineering, a turn also adopted by WHO in its Laboratory Biosafety Manual 4th Edition[13] and reasoned by Kojima *et al.*[14], with respect to the third edition of its WHO's Manual[15].

Costs are an opportunity, too

High and Maximum Biocontainment units are magnets for unique research, and technology and design transfer, and require highly trained technical personnel in biological risk management. In fact, biological risk and its management must be the driving force and leitmotif of the unit, even if the outputs are measured in scientific results, patents, vaccine prototypes or therapeutic molecules. It is this staff, trained for months or years, that allows a facility, a country, to respond to epidemic contingencies. In the middle of a storm, the helmsman does not have to explain what the mizzen is or how to raise the foresail. Furthermore, a helmsman must have a ship to sail the sea.

Costs are an opportunity to gain sustainability, a relevant factor to consider[16]. The sustainability race has two lanes, at least, adjusting and improving the consumption of basic supplies and reducing the volume of waste, and reusing energy residues, taking into account, for example, that air recirculation is generally prohibited (it depends on a specific risk assessment, see UNE 171400)[17] and, on the other hand, increasing the use of these facilities, opening them to more procedures and research, which does not necessarily mean more personnel directly involved. Again, it is necessary to have trained personnel, and actively on a continuous basis, a way of being trained.

This implies reconciling flexibility, efficiency, and biosafety requirements, to make these facilities more flexible in the management of large equipment, without losing the necessary Biosafety and Biocontainment standard. Confocal microscopes, live image analyzers, cell sorting equipment, etc. outside these BSL3 units do not allow the study of HG3 and HG4 pathogens[18], which are the usual causes of emerging or re-emerging infections (zoonotic or not). They must be installed inside and given intensive use, and the conjunction is difficult. For most genomic techniques there are methods for safely extracting samples from Biocontainment allowing the location of this equipment in unclassified areas.

Therefore, it is necessary to work on both levers; the lever of costs on a continuous and daily basis, because savings tend to be incremental and often procedural; that of opening access in a more discreet way, to maintain one's own activities and with a prior scientific and biosafety assessment.

Absence of clear standards and European or international regulation

There are significant variations in construction standards, management requirements, staff capacity and supervision procedures in these facilities. It is difficult to believe or accept but there is no clear standard of Biocontainment or International Biosafety[19] that is commonly accepted. It would be necessary to develop a global network of these facilities with a view to harmonizing construction standards, improving biosafety management systems, exchanging operational experiences, sharing personnel training resources, and applying a shared and transparent operational management concept. To give a close and personal example, until 2019 there was no design standard for level 3 biological containment facilities in Spain (the current UNE 171400-2019[17,20]). It is not mandatory to comply with, but it sets out minimum requirements, of a conceptual nature, discussed and agreed upon by technical and management experts on the field. And regarding risk management, perhaps the way forward would be to apply the 2019 International Organization for Standardization biological risk management standard for laboratories[21] as has been previously proposed[22] with third-party companies responsible for certification and validation.

Conclusion

Emerging and re-emerging infections will continue to challenge public and animal health systems. While basic molecular or immunological diagnostic procedures may often be performed in BSL2 laboratories after appropriate risk assessment and additional safety measures (PPE, personal restriction of access, stricter disinfection and waste management procedures), propagative work and animal experimentation with high-risk pathogens require active High or Maximum Biocontainment facilities and trained personnel. Since not every institution or region can independently build and maintain such infrastructure, reasonable open-access models are essential. The challenge is to make these facilities safer, more efficient, more sustainable, and more accessible, while preserving the necessary balance between biosafety and biosecurity. It's the Safe Grail that we are looking for.

Bibliography

1. Jones KE, Pate NG, Lev MA, Storeygard A, Balk D, Gittleman JL, *et al*. Global trends in emerging infectious diseases. *Nature*. 2008;451(7181):990-3. doi: 10.1038/nature06536.
2. Peters A. The global proliferation of high-containment biological laboratories: understanding the phenomenon and its implications. Rev Sci Tech. 2018;37(3):857-83. doi: 10.20506/37.3.2892.
3. Global Biolabs. Global Biolabs Report 2023. 2024. Available at: https://static1.squarespace.com/static/62fa334a3a6fe8320f5dcf7e/t/6412d3120ee69a4f4efbec1f/1678955285754/KCL0680_BioLabs+Report_Digital.pdf
4. Yeh KB, Tabynov K, Parekh FK, Mombo I, Parker K, Tabynov K, *et al*. Significance of High-Containment Biological Laboratories Performing Work During the COVID-19 Pandemic: Biosafety Level-3 and -4 Labs. *Front Bioeng Biotechnol*. 2021;(9):720315. doi: 10.3389/fbioe.2021.720315.
5. Muluneh AG, Moa A, Lim S, MacIntyre CR. Mapping biosafety level 3 (BSL-3) and BSL-4 laboratories for públic health threats reduction. *J Public Health*. 2025; doi: 10.1007/s10389-025-02492-3.
6. Boletín Oficial del Estado (2021). BOE-B-2021-28559. Redacción de proyecto y ejecución de las obras de construcción de laboratorio de contención biológica de nivel 4 en el campus del ISCIII en Majadahonda. Expediente: OM0020/2021. BOE núm. 135, de 7 de junio de 2021, pages 37231-32233. Available at: https://www.boe.es/diario_boe/txt.php?id=BOE-B-2021-28559
7. ISCIII. Memorandum y justificación para la construcción de un laboratorio de nivel cuatro de Bioseguridad (NBS-4) en el Centro Nacional de Microbiologia (CNM) del Campus de Majadahonda, Madrid del Instituto de Salud Carlos III. Available at: https://www.isciii.es/documents/20119/534638/Justificaci%C3%B3n+para+la+construcci%C3%B3n+de+un+laboratorio+de+nivel+de+bioseguridad+4+en+el+ISCIII.pdf/8d9c1256-d0f0-6e0d-6dd5-21a07662f30a
8. Animal's Health, 2025. El Gobierno aprueba el Laboratorio de Nivel de Contención Biológica 4 en el INIA-CISA por más de 22 millones de euros. Available at: https://www.animalshealth.es/politica/gobierno-aprueba-laboratorio-nivel-contencion-biologica-4-inia-cisa-mas-22-millones-euros
9. Halwe NJ, Cool K, Breithaupt A, Schön J, Trujillo JD, Nooruzzaman M, *et al*. H5N1 clade 2.3.4.4b dynamics in experimentally infected calves and cows. *Nature*. 2025;637:903-12. doi: 10.1038/s41586-024-08063-y.
10. Le Duc JW. Biocontainment Laboratories: A Critical Component of the US Bioeconomy in Need of Attention. *Health Security*. 2020;18(1):61-6. doi: 10.1089/hs.2020.0002.
11. World Health Organization. (2018). WHO consultative meeting high/màximum containment (biosafety level 4) laboratories networking,

13-15 December 2017: meeting report. 2018. Available at: https://apps.who.int/iris/handle/10665/311625

12. Abad X. Biocontainment in Low Income Countries: A Short Discussion. *Med Saf Glob Health*. 2018;7:139. doi: 10.4172/2574-0407/1000139.
13. WHO. Laboratory Biosafety Manual, 4th Edition. 2020. Available at: https://www.who.int/publications/i/item/9789240011311
14. Kojima K, Makison C Booth, Summermatter K, Bennett A, Heisz M, *et al*. Risk-based reboot for global lab biosafety: New WHO guidance could expand access to lab facilities. *Science*. 2018;360(6386):260-2. doi: 10.1126/science.aar2231.
15. WHO. Laboratory Biosafety Manual, 3th Edition, Geneva. 2004. Available at: https://www.who.int/publications/i/item/9241546506
16. Xia H, Yuan Z. High-containment facilities and the role they play in global Health security. *J Biosafety and Biosecurity*. 2022;(4):1-4. doi: 10.1016/j.jobb.2021.11.005.
17. AENOR (2019). UNE 171400-1-2019 Diseño de Instalaciones de nivel 3 de contención biológica. Available at: https://tienda.aenor.com/p/norma-une-171400-1-2019-n0062375
18. Boletin Oficial del Estado (1997). BOE-A-1997-11144. Real Decreto 664/1997, de 12 de mayo, sobre la protección de los trabajadores contra los riesgos relacionados con la exposición a agentes biológicos durante el trabajo. BOE núm. 124, de 24/05/1997.
19. Silver A. Why the world has no universal biosafety standards. *BMJ*. 2022;377:o954. doi: 10.1136/bmj.o954.
20. Usera F. La Norma UNE 171400-1:2019 Diseño de Instalaciones de Nivel 3 de Contención Biológica (NCB3). *Revista SECAL, Animales de Laboratorio*. 2021;81:44-8. Available at: https://aebios.org/wp-content/uploads/2021/04/SECAL-REVISTA-81r.pdf
21. ISO 35001:2019(es). Gestión del riesgo biológico en laboratorios y otras organizaciones relacionades. Available at: https://www.iso.org/obp/ui/es/#iso:std:iso:35001:ed-1:v1:es
22. Rodgers J, Lentos F, Koblentz GD, Ly M. How to make sure the labs researching the most dangerous pathogens are safe and secure. *Bull At Sci*. 2021; Available at: https://thebulletin.org/2021/07/how-to-make-sure-the-labs-researching-the-most-dangerous-pathogens-are-safe-and-secure/