中央研究院
ACADEMIA SINICA

實驗室生物安全：
生物實驗室及生物材料庫負責人之核心責任

生安辦公室執行長 吳文超

2024.4.8




您的實驗室安全嗎?

文獻回顧_1/5

Laboratory-acquired infections and pathogen escapes worldwide between 2000 and 2021: a scoping review

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The Lancet Microbe
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2000 年至 2021 年間全球實驗室感染（Laboratory-acquired infections, LAIs）及實驗室病原體意外洩漏（accidental pathogen escape from laboratory settings, APELS）研究調查

https://www.thelancet.com/action/showPdf?pii=S2666-5247(23)00319-1

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文獻回顧_2/5

	N cases	N fatalities†
Bacteria		
Salmonella Typhimurium	154 (49·8%)	1 (12·5%)
Salmonella enteritidis	21 (6·8%)	
Brucella spp*	12 (3·9%)	
Brucella melitensis	11 (3·6%)	
Neisseria meningitidis	7 (2·3%)	3 (37·5%)
Escherichia coli O157:H7	6 (1·9%)	
Francisella tularensis	4 (1·3%)	
Brucella suis	3 (1·0%)	
Salmonella Typhi	3 (1·0%)	
Staphylococcus aureus	2 (0·7%)	
Yersinia pestis	2 (0·7%)	2 (25·0%)
Bacillus anthracis	1 (0·3%)	
Bacillus cereus	1 (0·3%)	
Brucella abortus	1 (0·3%)	
Brucella canis	1 (0·3%)	
Burkholderia mallei	1 (0·3%)	
Campylobacter jejuni	1 (0·3%)	
Klebsiella (Enterobacter) aerogenes	1 (0·3%)	
Leptospira spp	1 (0·3%)	
Mycobacterium tuberculosis	1 (0·3%)	
Neisseria gonorrhoeae	1 (0·3%)	
Orientia tsutsugamushi	1 (0·3%)	
Shigella spp	1 (0·3%)	
Vibrio cholerae	1 (0·3%)	
Sub-total	238 (77·0%)	6 (75·0%)
Virus		
Vaccinia virus	13 (4·2%)	
Zika virus	5 (1·6%)	
Dengue virus	4 (1·3%)	
SARS-CoV	4 (1·3%)	
HIV	3 (1·0%)	
Crimean Congo haemorrhagic fever virus	2 (0·7%)	
West Nile virus	2 (0·7%)	
Buffalo pox virus	1 (0·3%)	
Cowpox virus	1 (0·3%)	
Ebola virus	1 (0·3%)	1 (12·5%)
Influenza virus	1 (0·3%)	
Lymphocytic choriomeningitis virus	1 (0·3%)	
Mimivirus	1 (0·3%)	
Norovirus	1 (0·3%)	
Poliovirus	1 (0·3%)	
Recombinant raccoonpox virus	1 (0·3%)	
SARS-CoV-2	1 (0·3%)	
Subtotal	43 (13·9%)	1 (12·5%)
Parasite		
Cryptosporidium spp	16 (5·2%)	
Toxoplasma gondii	3 (1·0%)	
Echinococcus spp	1 (0·3%)	
Leishmania (Viannia) naiffi	1 (0·3%)	
Plasmodium vivax	1 (0·3%)	
Sub-total	22 (7·1%)	0

(Table 2 continues in next column)

(Continued from previous column)

	N cases	N fatalities†
Fungus		
Sporothrix schenckii	2 (0·7%)	
Arthroderma benhamiae	1 (0·3%)	
Coccidioides spp	1 (0·3%)	
Histoplasma capsulatum var *capsulatum*	1 (0·3%)	
Subtotal	5 (1·6%)	0
Prion		
Bovine spongiform encephalopathy	1 (0·3%)	1 (12·5%)
Total	309 (100·0%)	8 (100%)

LAI=laboratory-acquired infection. *The *Brucella* species causing the LAI was not stated in the report. †Derived from LAI case report.

Table 2: **Causal pathogens for the LAI cases and fatalities**



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文獻回顧_3/5

	Date	Location	Facility	APELS category	Exposures (n)	Cases (n*)	Cause	Reference(s)
Bacillus anthracis	June, 2014	US Centres for Disease Control and Prevention, Bioterrorism Rapid Response and Advanced Technology, GA, USA	Research	Internal	Not stated	0	Procedural error	24
	April–May, 2015	Dugway Proving Ground, UT, USA	Research	External	Not stated	0	Procedural error	25,26
	May, 2012	Animal Health and Veterinary Laboratories Agency, Surrey, UK	Research	External	2	0	Procedural error	27,28
SARS-CoV	August, 2003	National University of Singapore and Environmental Health Institute of Singapore, Singapore	Research	External	84	1	Procedural error	3,29,30
	December, 2003	Taiwan Military Institute of Preventive Medical Research of the National Defence University, Sanxia, Taiwan	Research	External	74	1	Procedural error	3,29,31
	April, 2004	Chinese National Institute of Virology, Beijing, China	Research	External	747	11	Procedural error	3,29,32
Foot and mouth disease virus	June, 2004	Plum Island Animal Disease Center, NY, USA	Research	Internal	Not stated	6 cattle/pigs	Not stated	33
	August, 2007	Pirbright, Surrey, UK	Research	External	Not stated	Not stated	Engineering	2,34
Brucella spp	Mid-2019	Lanzhou, China	Vaccine	External	Not stated	10 528	Procedural error	5,35,36
	2018	USA, location unknown	Not stated	External	Not stated	Not stated	Not stated	37
Influenza virus	January, 2014	Southeast Poultry Research Laboratory, GA, USA	Research	External	Not stated	0	Procedural error	38
Variola virus	July, 2014	National Institutes of Health, MD, USA	Research	Internal	Not stated	0	Procedural error	39
Burkholderia pseudomallei	Mid-January, 2015	Tulane National Primate Research Center, LA, USA	Research	Internal	Not stated	2 primates	Procedural error	40
Poliovirus	September, 2000; November, 2002–February, 2003	India	Vaccine	External	Not stated	8 or 10	Not stated	41,42
	September, 2014	Belgium	Vaccine	External	Not stated	Not stated	Not stated	43
	April, 2017	Netherlands	Vaccine	External	2	0	Not stated	44

APELS=accidental pathogen escape from laboratory settings. *If not stated explicitly, the data presented refer to human cases.

***Table 3*: Pathogens associated with internal and external APELS**

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文獻回顧_4/5

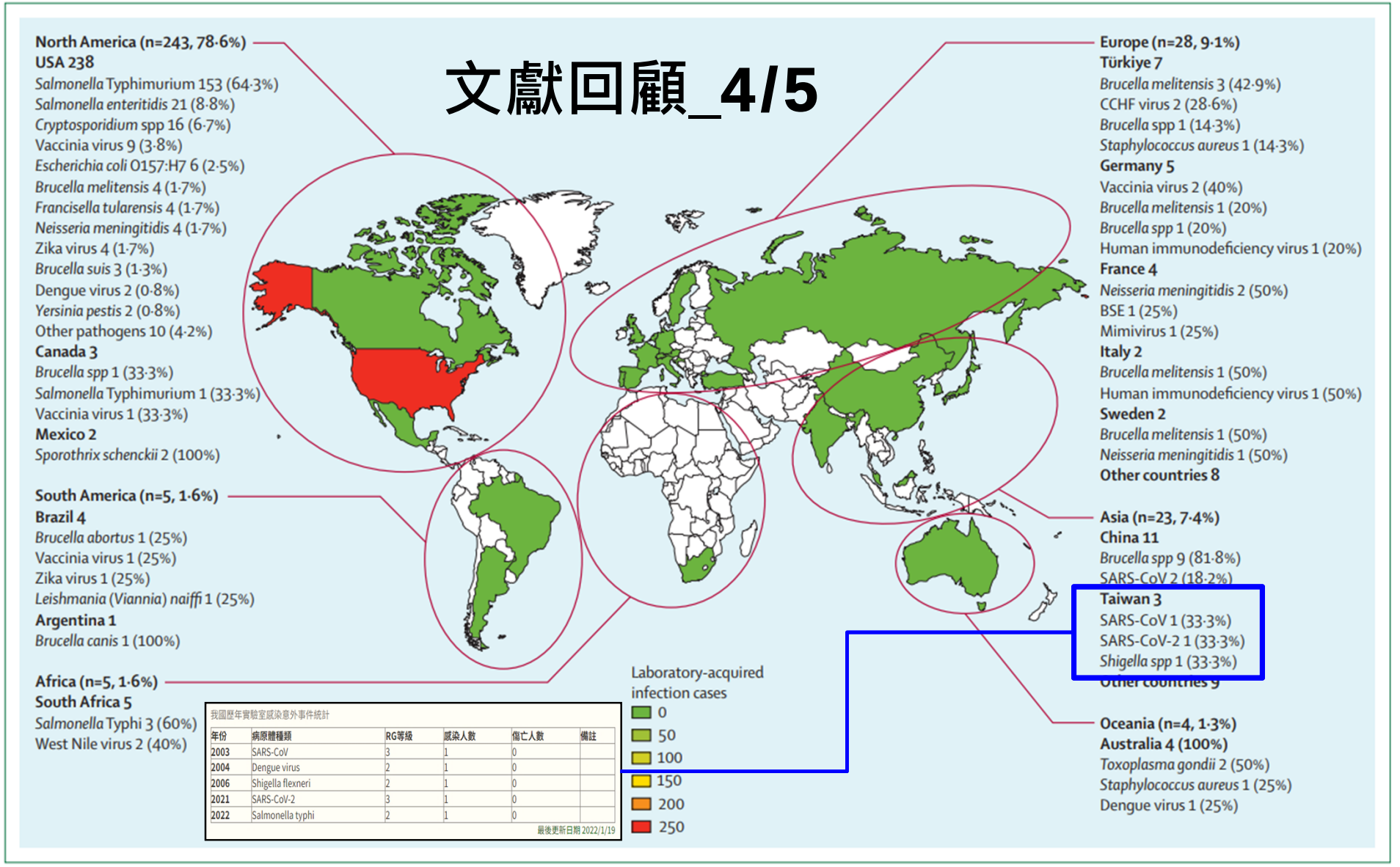


Figure 1: **Laboratory-acquired infection case reports, including causal pathogens for each geographical region for the period from 2000 to 2021. Note that in 1 instance the geographic location of the LAI case was not stated.**

文獻回顧_5/5

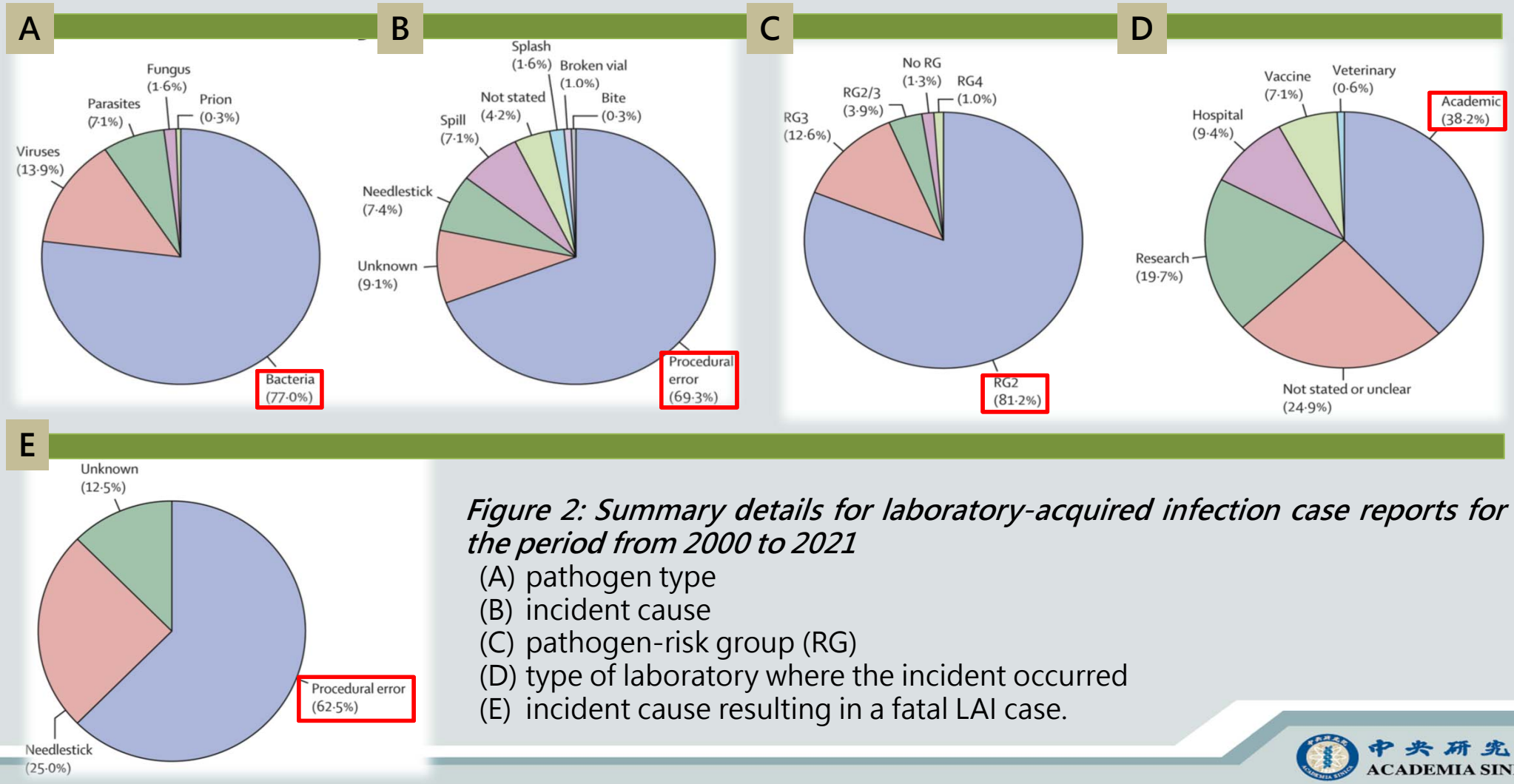


Figure 2: Summary details for laboratory-acquired infection case reports for the period from 2000 to 2021

(A) pathogen type
(B) incident cause
(C) pathogen-risk group (RG)
(D) type of laboratory where the incident occurred
(E) incident cause resulting in a fatal LAI case.

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全球歷年LAI 調查統計

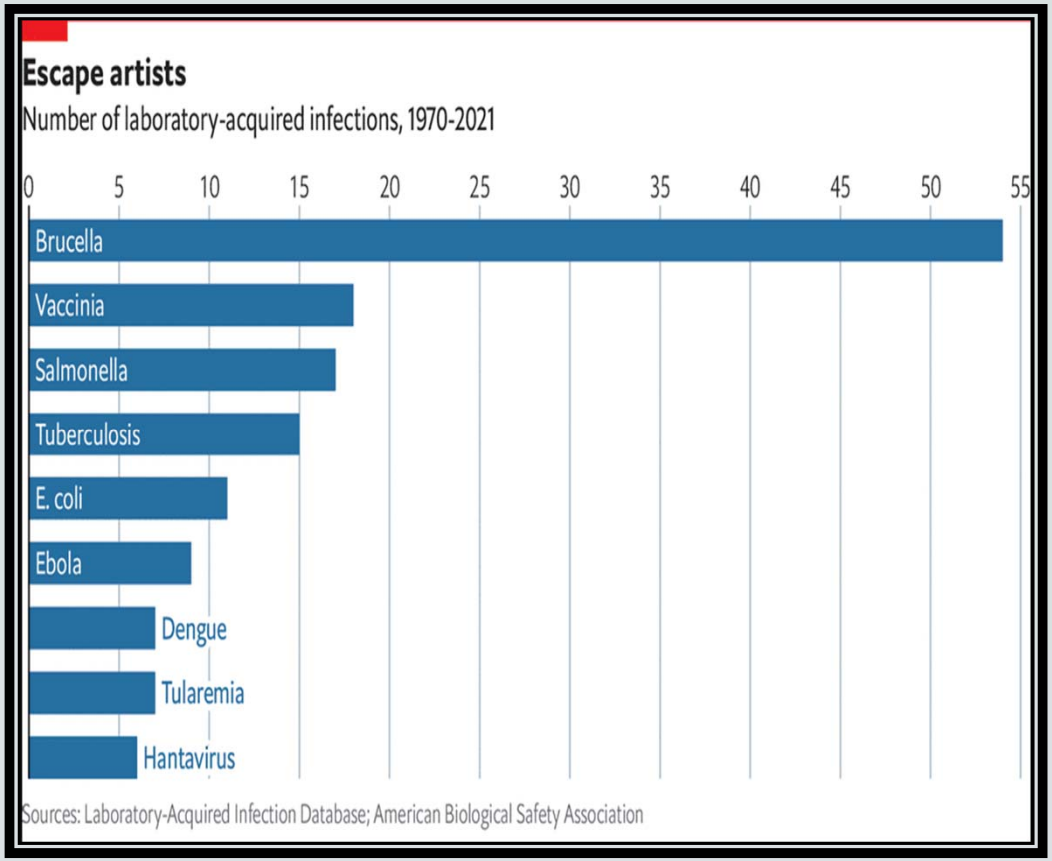
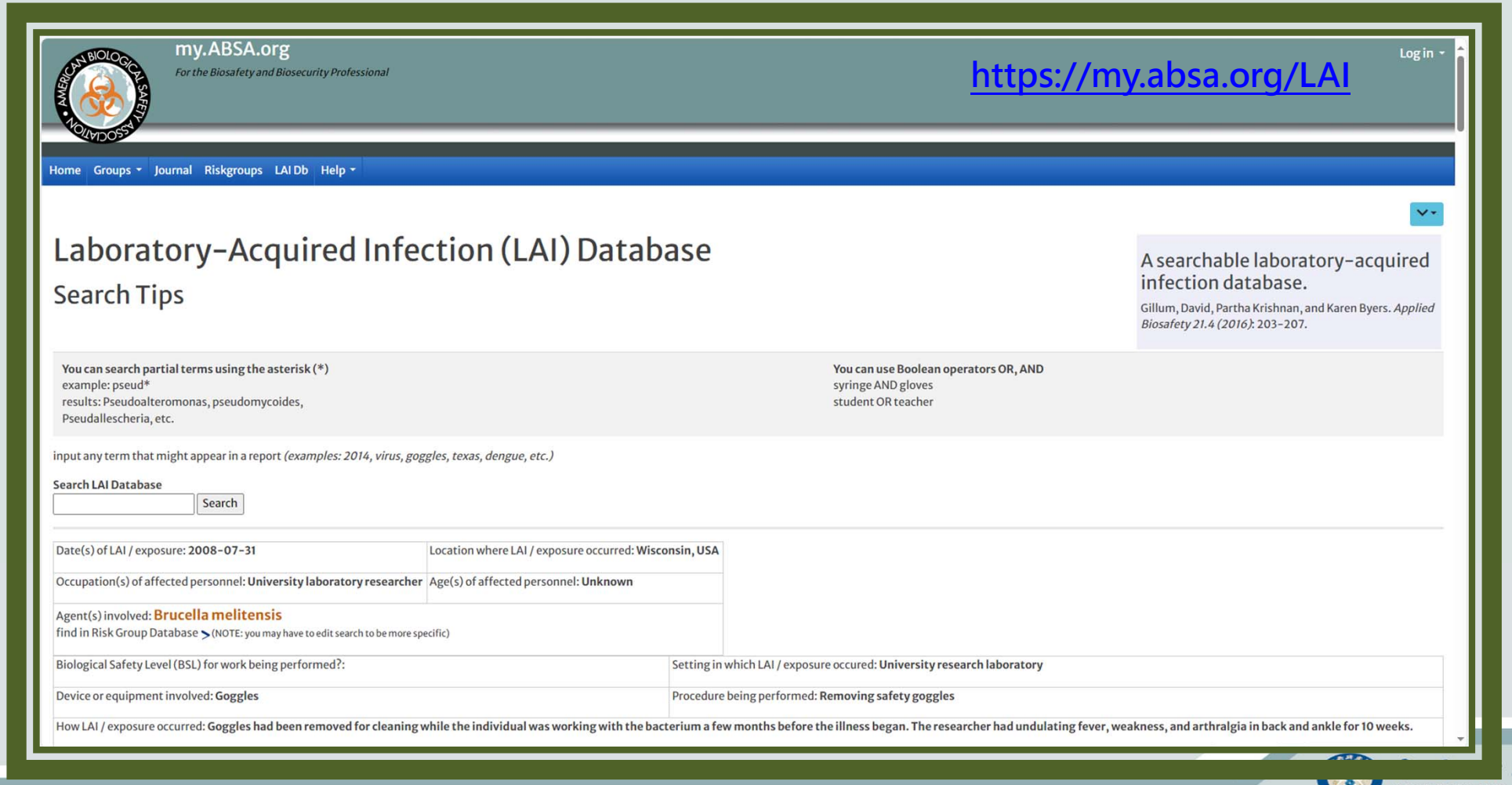


Table 1 : "Top ten" laboratory-acquired infections (1979-1999)
Adapted from Collins, 1998 and Harding & Brandt Byers, 2000

Biological agent *(with links, when available, to the corresponding Material Safety Data Sheet (MSDS) from the Office of Laboratory Security, Health Canada*	Class of risk or risk group *Classes of risk are given for human. More information on this page*	Disease
Brucella spp.	3	Brucellosis
Coxiella burnetii	3	Q fever
Hepatitis B, C and D viruses	3 *(class of risk 3 infectious agents that are normally not airborne pathogens)*	Hepatitis
Salmonella thyphi	3 *(class of risk 3 infectious agents that are normally not airborne pathogens)*	Typhoid fever
Francisella tularensis	3	Tularaemia
Mycobacterium tuberculosis complex	3	Tuberculosis
Trycophyton mentagrophytes	2	Dermatomycosis
Venuzeelan equine encephalitis virus	3	Venezuelan equine encephalitis
Chlamydia psittaci (avian)	3	Psittacosis
Coccidioides immitis	3	Coccidioidomycosis

https://www.biosafety.be/content/laboratory-acquired-infections-and-bio-incidents

美國生物安全協會(ABSA) LAI 資料庫



前車之鑑，後事之師

- **案件描述**

  民國110年12月9日中央研究院動物生物安全第三等級實驗室(ABSL-3實驗室)工作人員發生感染SARS-CoV-2事件。

- **後續改善**
  - 強化生物安全會之功能及職責
  - 檢討ABSL-3實驗室現行生物安全規範與標準作業程序適切性
  - 訂定生物安全內部稽核規範並落實執行
  - 建立實驗室人員適任性評核/知能評核基準
  - 強化工作人員教育訓練情形查驗制度
  - 建立實驗室意外及異常事件主動追蹤監測機制
  - 訂定工作人員健康監測計畫

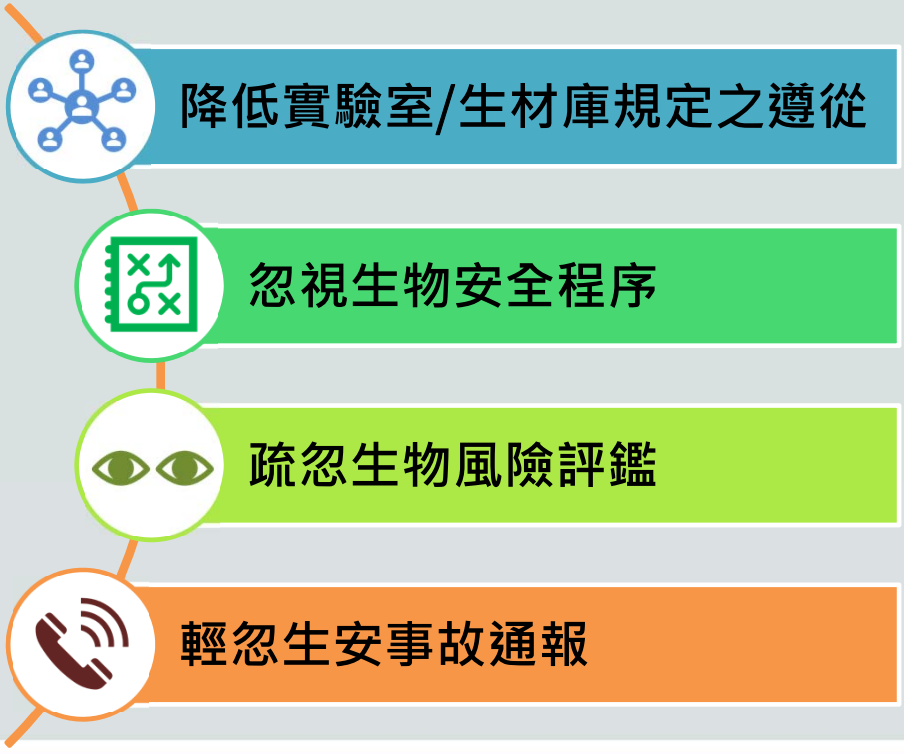


LAI事件的代價

人員	實驗室	設置單位	社區民眾
• 心理壓力 • 健康損失 • 遭受懲處 • 工作阻礙	• 營運損失 • 資產損失 • 研究受阻	• 聲譽損失 • 法律責任 • 遭受裁罰	• 民眾健康 • 民眾信任

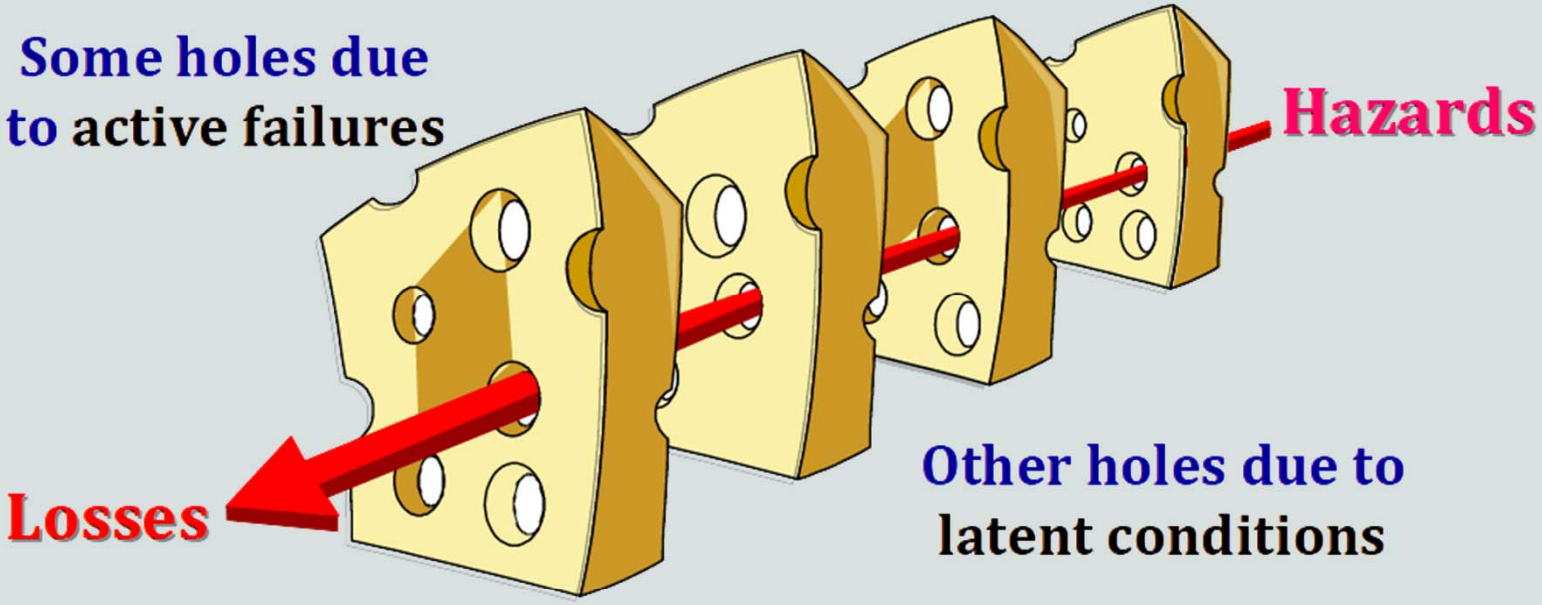
這不會發生在我的實驗室/生材庫!

- **過度自信心態**：可能源於過去無事故之發生、自恃經驗豐富，導致實驗室人員認為對於實驗室潛在危險有足夠之控制及理解，從而降低對安全措施之重視，包括：



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Swiss Cheese Model Of Accident Causation
(意外因果的瑞士乳酪模型)



“無事故”不等於“無風險”

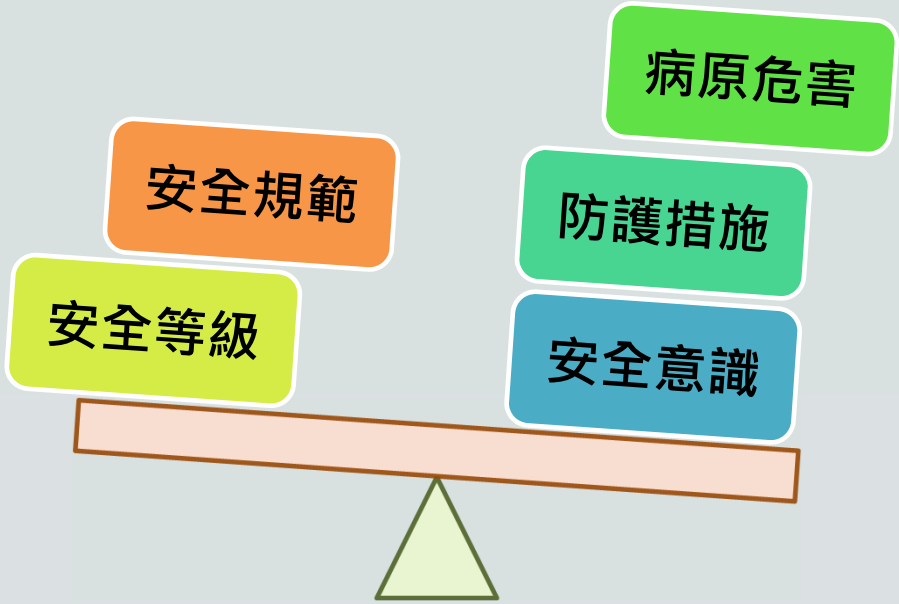
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您認為二級還是三級實驗室比較危險?

BSL-2/
ABSL-2

VS.

BSL-3/
ABSL-3





RG1微生物在二級實驗室操作之SWOT分析



優勢(S)

- 未來準備
- 提升安全
- 提升品質

弱點(W)

- 運作成本
- 訓練要求
- 內稽要求

機會(O)

- 擴展研發
- 吸引人才
- 因應時勢

威脅(T)

- 資源浪費
- 遵從挑戰
- 誤解風險

實驗室/生材庫負責人在生物安全之責任

1. 遵循單位生安政策及規定
2. 實施生物風險評鑑
3. 訂定及更新生安手冊及程序
4. 落實生安教育訓練
5. 提供並確保防護裝(設)備之有效及安全
6. 落實生物病原保全管理
7. 落實年度生安內部稽核
8. 落實應變計畫演習及事故通報

1.遵循單位生安政策及規定

- 本院生安會網址：https://biosafety.sinica.edu.tw/



2.實施生物風險評鑑_1/3

- 風險評鑑模板及資源
  - WHO: https://www.who.int/publications/i/item/9789240011458
  - 加拿大PHAC: https://www.canada.ca/en/public-health/services/canadian-biosafety-standards-guidelines/guidance.html

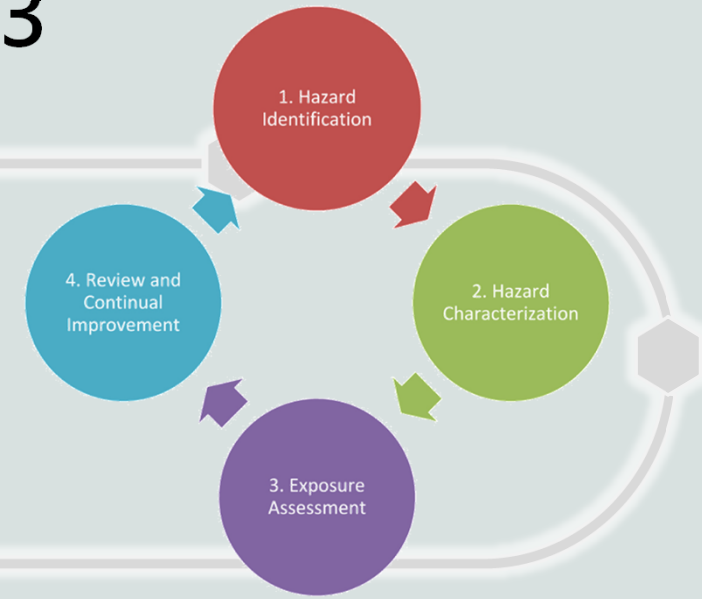


2.實施生物風險評鑑_2/3

執行時機

- 新建實驗室
- 新進人員
- 新病原體
- 新程序或技術
- 新設備
- 發生事故/虛驚事件後
- 法規及規定變更
- 每年度





Step 1: Identify and Characterize Hazards
Step 2: Identify and Assess Risk
Step 3: Develop and Implement Risk Mitigation Strategies
Step 4: Review and Continually Improve

2.實施生物風險評鑑_3/3

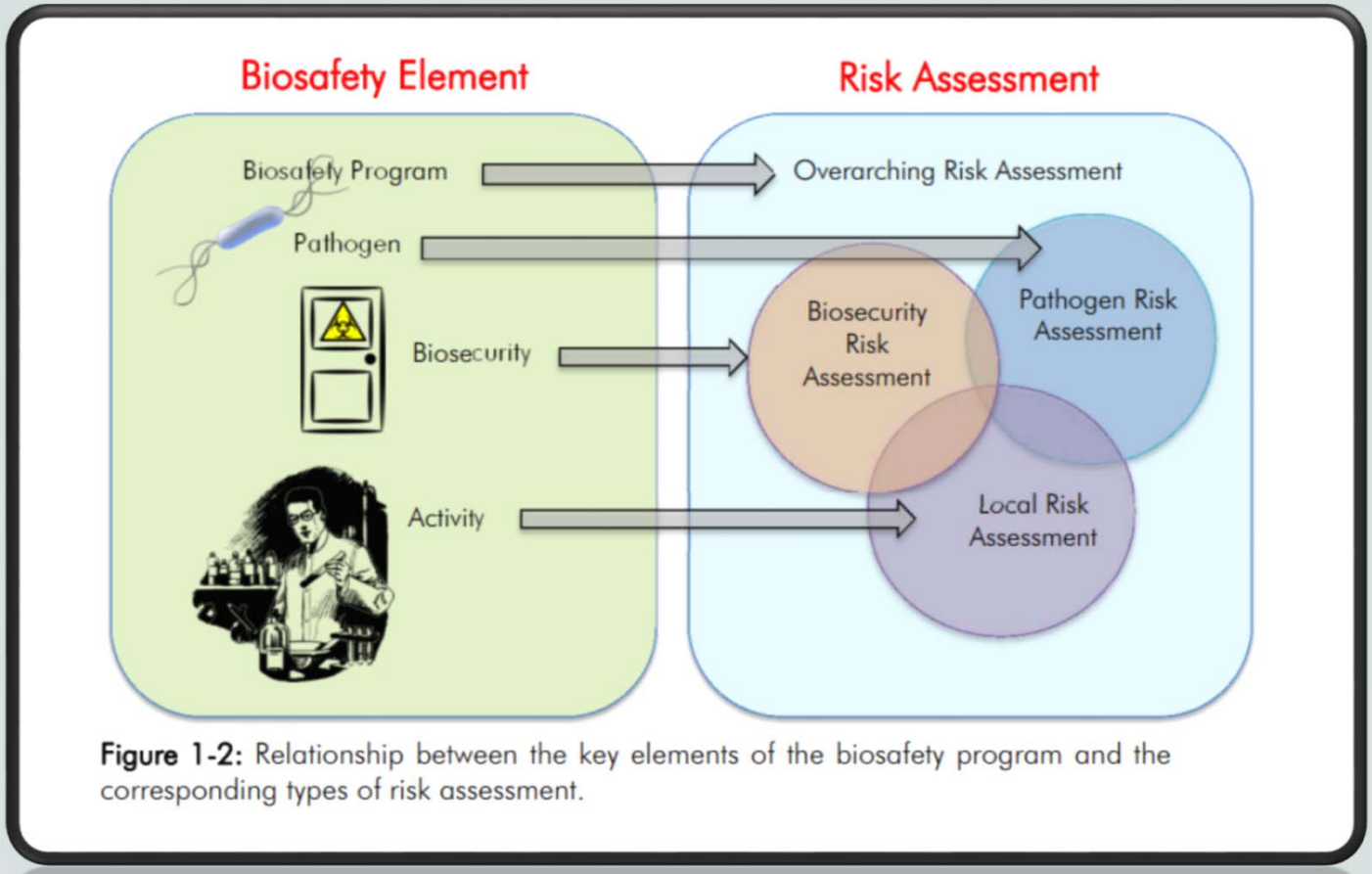
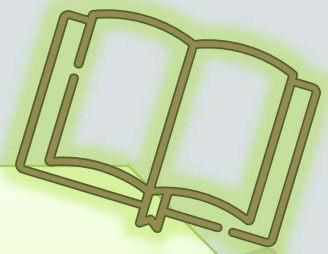


Figure 1-2: Relationship between the key elements of the biosafety program and the corresponding types of risk assessment.

Canadian Biosafety Guideline Pathogen Risk Assessment

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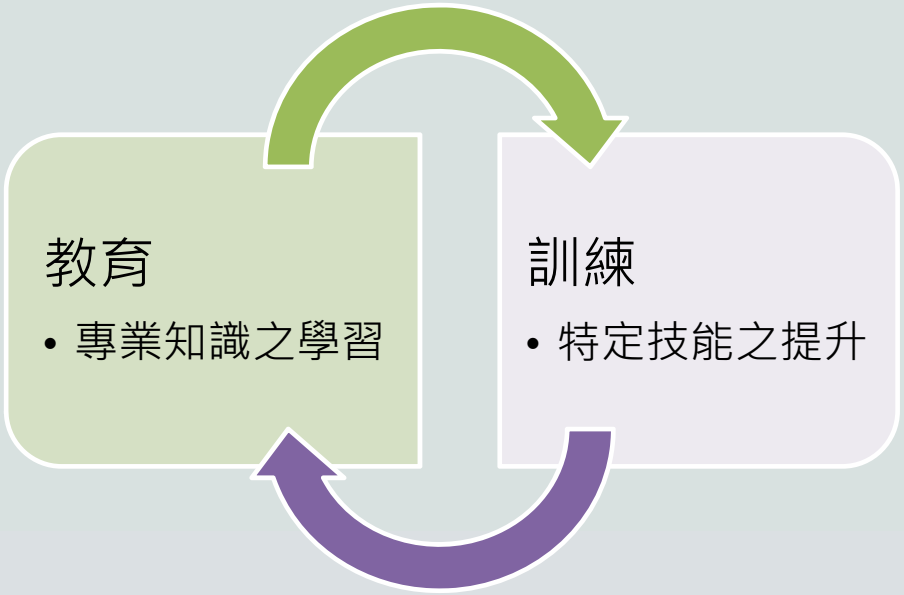
3.訂定及更新生安手冊及程序



- 實驗室生物安全手冊(WHO範本)

1. Overview and purpose
2. Scope
3. Definition of terms
4. Institutional policies
5. Roles and responsibilities
6. Operational working practices
7. Records and documentation
8. Personnel competence and training
9. Risk control measures
10. Waste management
11. Biosecurity plan
12. Emergency/incident response
13. Occupational health programme
14. Transport and shipment of biological materials
15. Internal and external audits and inspections
16. Laboratory decommissioning

4.落實生安教育訓練_1/4



4.落實生安教育訓練_2/4

- 實驗室生安訓練方案



4.落實生安教育訓練_3/4

- 在職人員繼續教育的必要性

Laboratory-acquired infections in Canada, 2016 to 2021

Table 1: Descriptions of each of the nine confirmed laboratory-acquired infections in the Laboratory Inci surveillance system, Canada, 2016–2021

Variable	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Role	Student	Technician	Technician	Technician	Technician	Technician	Technician
Highest degree	Master's Degree	Technical diploma	Bachelor's degree	Bachelor's degree	Bachelor's degree	Technical diploma	Bachelor's degree
Years of experience	Fewer than 5	Fewer than 5	Unknown	Fewer than 5	10–20	5–10	5–10
Laboratory type	Academic	Hospital	Government Public Health	Hospital	Government Public Health	Hospital	Academic
Main work activity	*In vivo* animal work	Microbiology	Microscopy	Microbiology	Microbiology	Microbiology	Animal care
Biological agent	*Staphylococcus aureus*	*Salmonella* spp.	*Salmonella* spp.	*Brucella* spp.	*Salmonella* spp.	*E. coli*	*Vaccinia virus*

4.落實生安教育訓練_4/4

電子公文

檔　　號：
保存年限：

衛生福利部疾病管制署　函

機關地址：10050台北市中正區林森南路6號
聯絡人：陳奕禎
聯絡電話：02-23959825#3871
電子信箱：iameros@cdc.gov.tw

受文者：中央研究院

發文日期：中華民國108年1月19日
發文字號：疾管感字第1080030432號
速別：普通件
密等及解密條件或保密期限：
附件：

主旨：有關貴院函詢實驗室及保存場所之工作人員於「感染性生物材料管理辦法」第19條條文之適用疑義，復如說明段，請查照。

說明：

一、復貴院108年1月11日總務字第1080500287號函。

二、依據旨揭辦法第19條第2項規定，實驗室及保存場所之工作人員，每年應取得生物安全及生物保全繼續教育至少4小時。此規定所稱之工作人員，包括實驗室主管、管理人員及在實驗室及保存場所內工作之人員，合先敘明。

三、實驗室主管、管理人員負責實驗室及保存場所之監督或管理，理應了解及熟悉實驗室生物安全管理法規及要求。至於在實驗室及保存場所從事清潔或行政庶務之人員，雖未從事感染性生物材料操作，然處於暴露在生物病原潛在風險之環境，仍應具備生物安全及生物保全知識，避免因個人安全意識不足，出現違反規定之行為或舉動，造成生物危害意外。因此，前開人員每年皆應接受生物安全及生物保全繼續教育至少4小時。

正本：中央研究院
副本：電子公文交換章 2019/01/21 00:58:23

負責人之生物安全教育要求

電子公文

檔　　號：
保存年限：

中央研究院　書函

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電子信箱：chenchengnan@gate.sinica.edu.tw

受文者：本院總務處

發文日期：中華民國105年2月5日
發文字號：學術字第1050500784號
速別：普通件
密等及解密條件或保密期限：
附件：

主旨：有關本院104年度第3季生物安全會議決議之生物安全決策事項，並重申本院生物安全教育訓練規定，若未遵照規定經主管機關處罰者，應由實驗室負責人及當事人共同承擔，請查照轉知。

說明：

一、依「感染性生物材料管理辦法」第19條規定，實驗室新進人員應接受實驗室生物安全課程至少八小時；實驗室工作人員每年應取得實驗室生物安全持續教育至少四小時；生物安全第三等級以上實驗室新進人員，應參加中央主管機關認可之生物安全訓練。

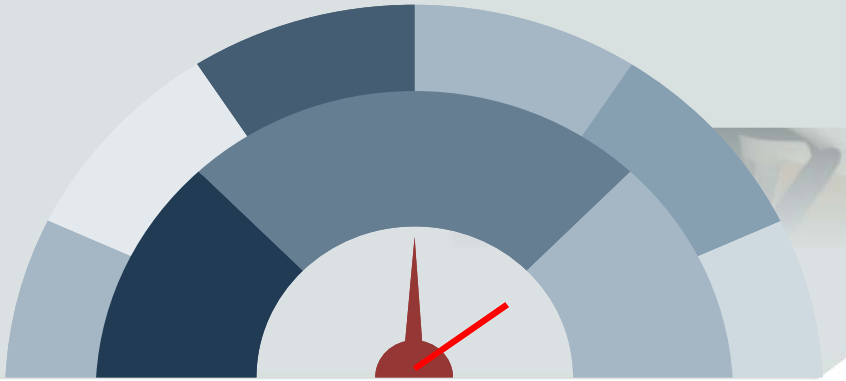
二、本院生物實驗室人員應受生物安全教育訓練之適用對象，以濕式生物實驗室（wet-lab）人員為主，說明如下：

（一）研究人員/研究技術人員（含實驗室負責人）。
（二）博士後研究員/研究助理。
（三）碩/博士研究生。
（四）實習生/暑期生。
（五）其他於檢驗、研究或相關工作可能接觸具生物危害之生醫廢棄物者。

三、前述人員應於每年年底前，應依規定完成生物安全教育訓練課程；未遵照規定經主管機關處罰者，應由實驗室負責

5.提供並確保防護裝(設)備之有效及安全_1/2

- 項目
  - **設施**—通風空調系統
  - **個人防護裝備**—PPE
  - **安全設備**—BSC(生材庫不適用)
  - **除汙設備**—高壓滅菌器
- 責任
  - 提供並教導人員正確選擇及使用
  - 確認定期功能檢測及確效
  - 確認定期保養維護



5.提供並確保防護裝(設)備之有效及安全_2/2

- **實驗室BSC爆炸事故**
  - 在伊拉克一所大學，一名研究生在開始進行涉及幹細胞實驗前，使用本生燈進行實驗器具或培養瓶消毒，當她點燃本生燈時，因BSC積聚液化石油氣(LPG)引起爆炸，造成當事人受傷，並引發火災。

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Laboratory biological safety cabinet (BSC) explosion

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Fig. 2. BSC with Bunsen burner inside.

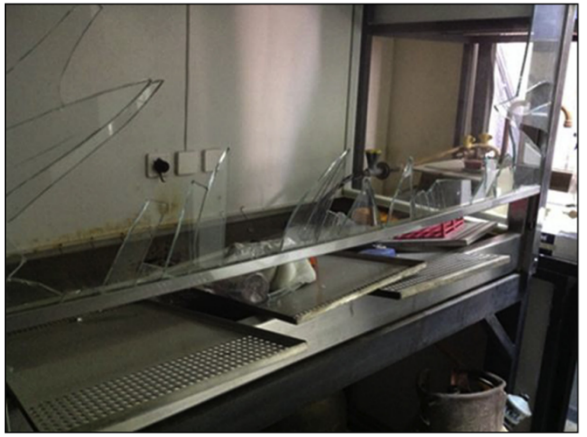


Fig. 1. Glass shards remain in the frame of the sash in this BSC after an explosion in a university laboratory.

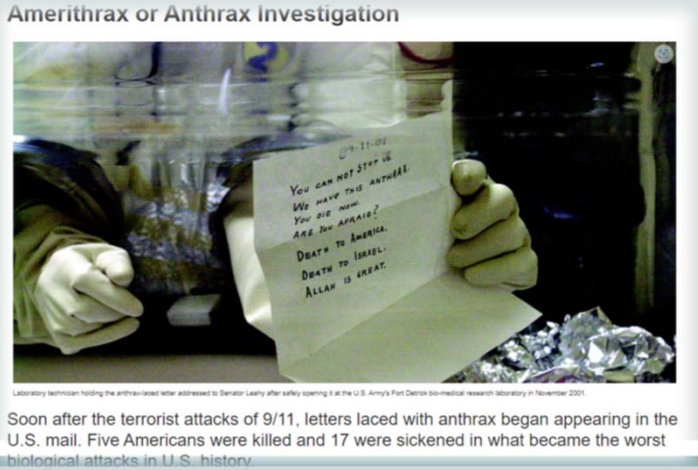
6.落實生物病原保全管理_1/2

- **2001年美國炭疽恐怖郵件事件**

  2001年，美國陸軍醫學研究院的傳染性病原體研究所（USAMRIID）在處理炭疽桿菌時出現漏洞，導致數封含有炭疽孢子的信件被發送至美國國內多個地點，造成5人死亡，17人感染。

- **2014年美國馬里蘭州天花病毒遺留事件**

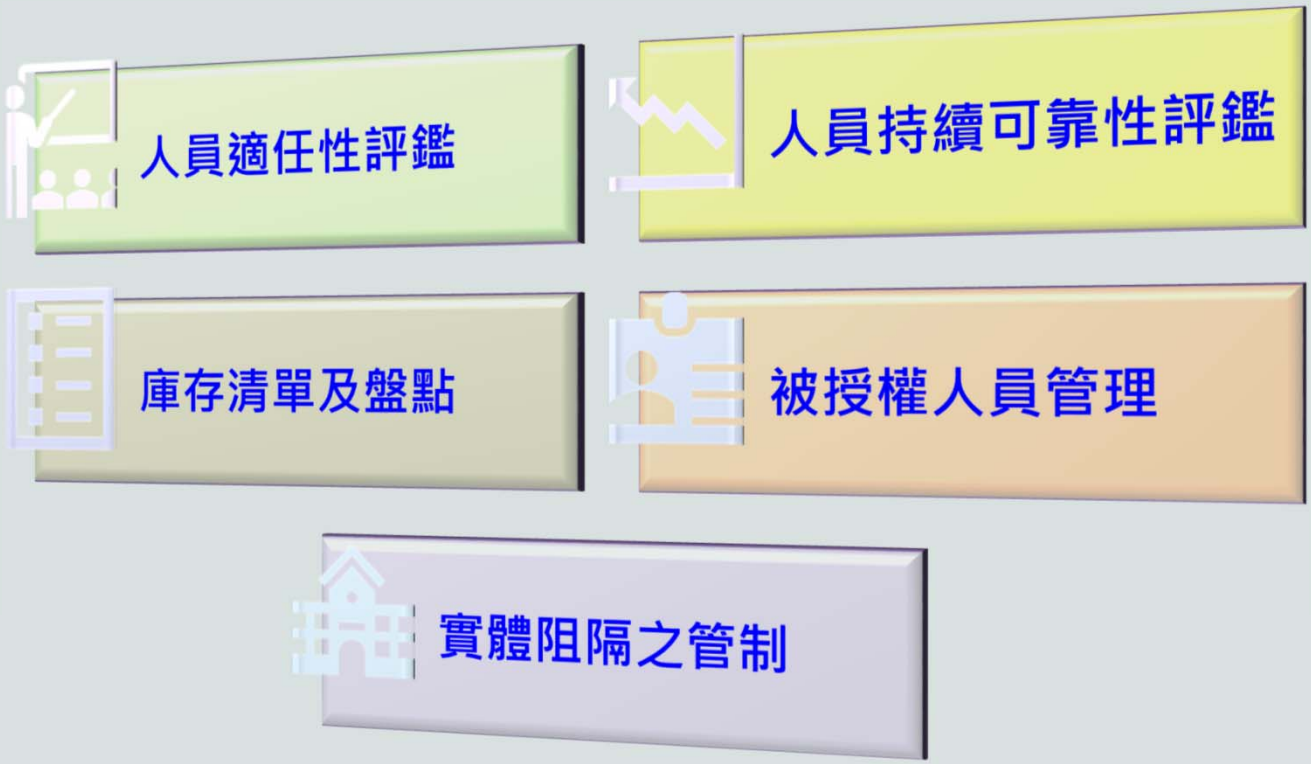
  2014年，美國食品藥物管理局位於馬里蘭州貝塞斯達的某實驗室，因進行搬遷時，於儲存室內發現6支標示”天花病毒”小管，經了解此為1972年美國國立衛生研究院所遺留。



Soon after the terrorist attacks of 9/11, letters laced with anthrax began appearing in the U.S. mail. Five Americans were killed and 17 were sickened in what became the worst biological attacks in U.S. history.

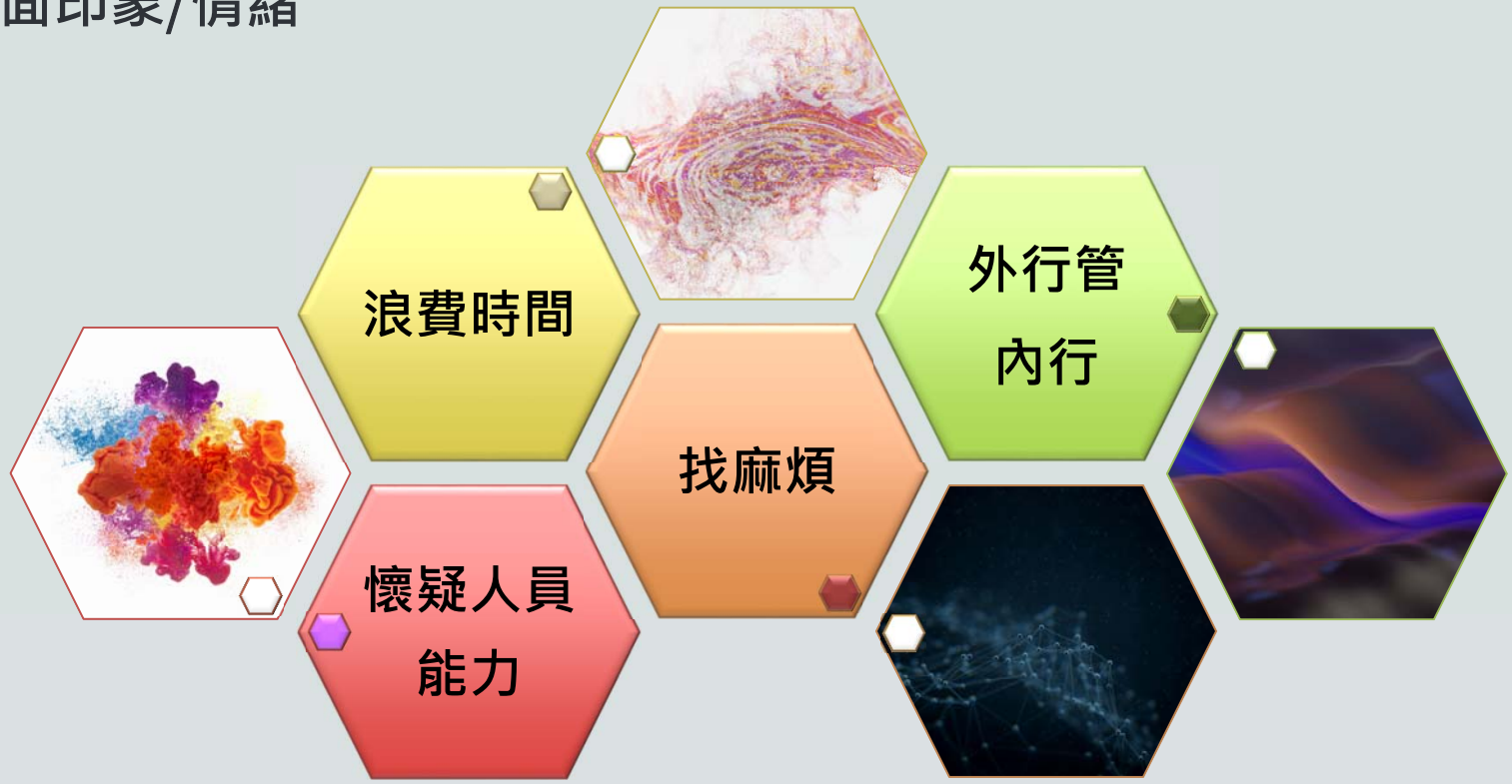


6.落實生物病原保全管理_2/2



7.落實年度生安內部稽核_1/3

- 常見負面印象/情緒



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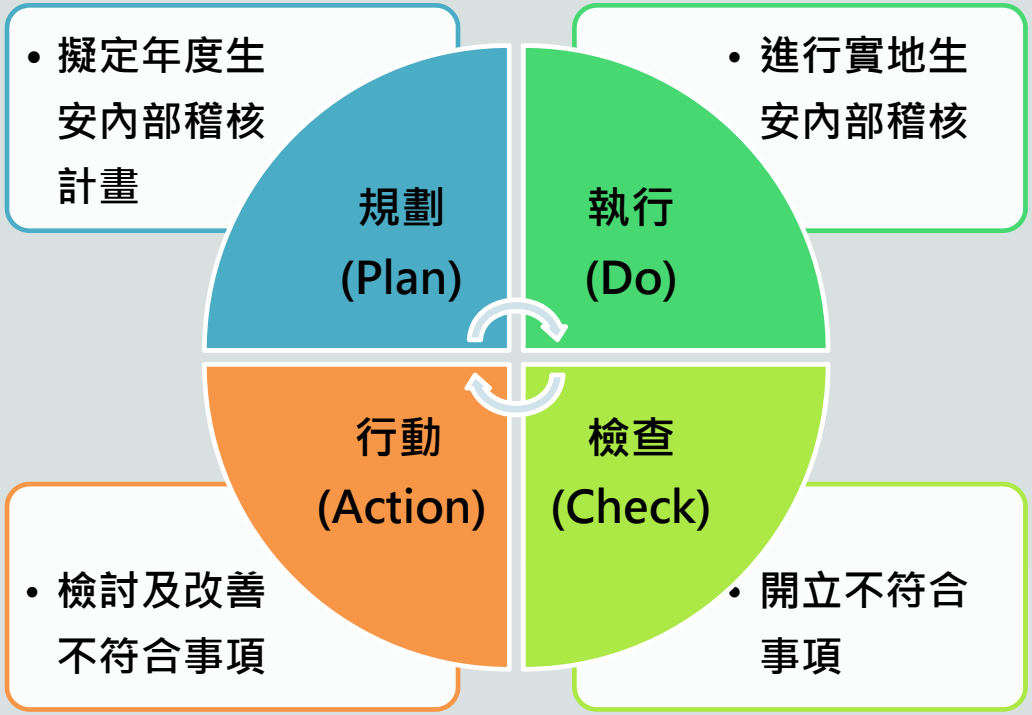
7.落實年度生安內部稽核_2/3

- 目的



7.執行年度生物安全內部稽核_3/3

- 方式



8.落實應變計畫演習及事故通報

- 重要性

確認
應變計畫
有效性

確認
應變物資
完整性

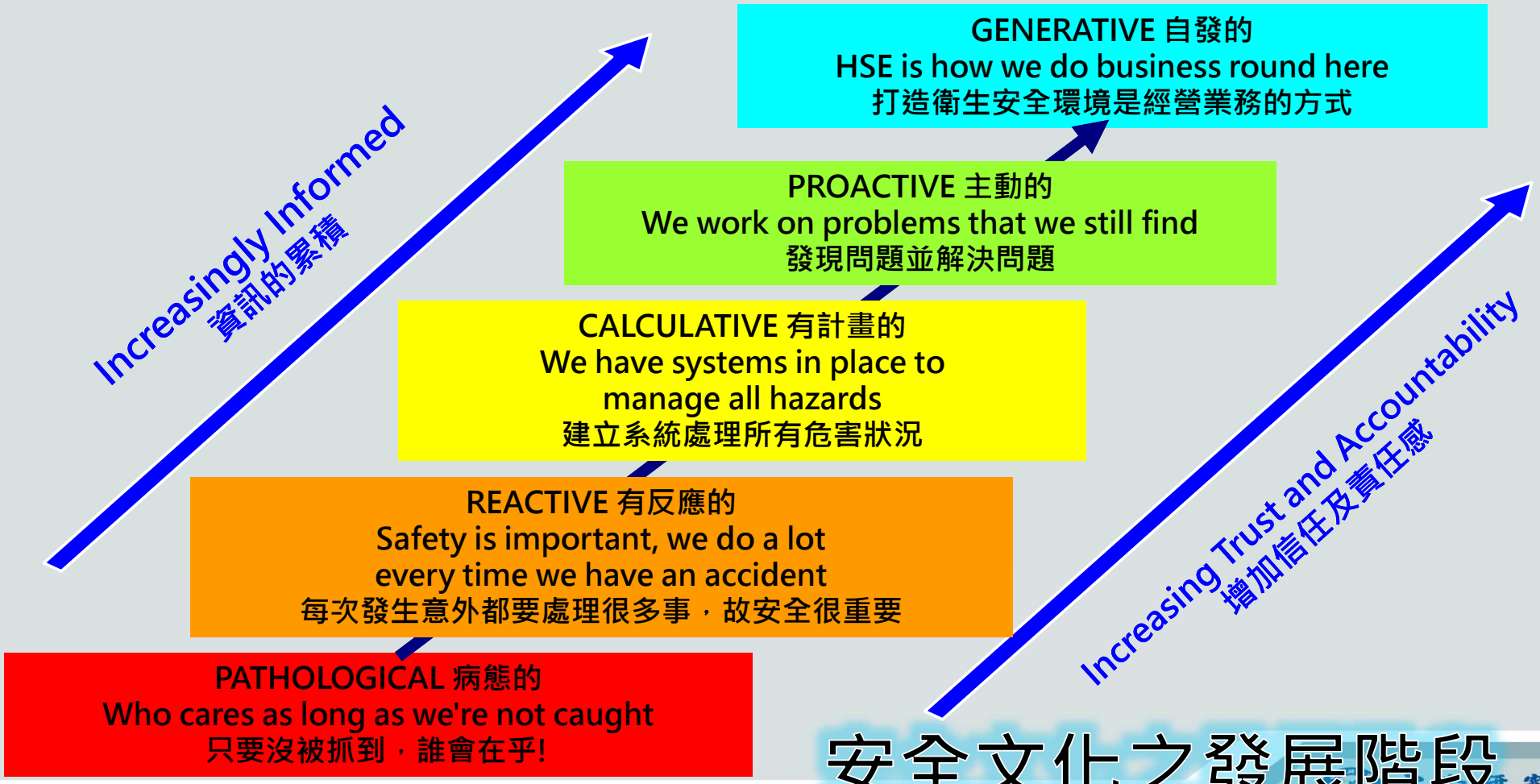
提高人員
應變意識
及能力

提升人員
團隊溝通
及協調

符合法規
要求



建立生物安全文化_1/3

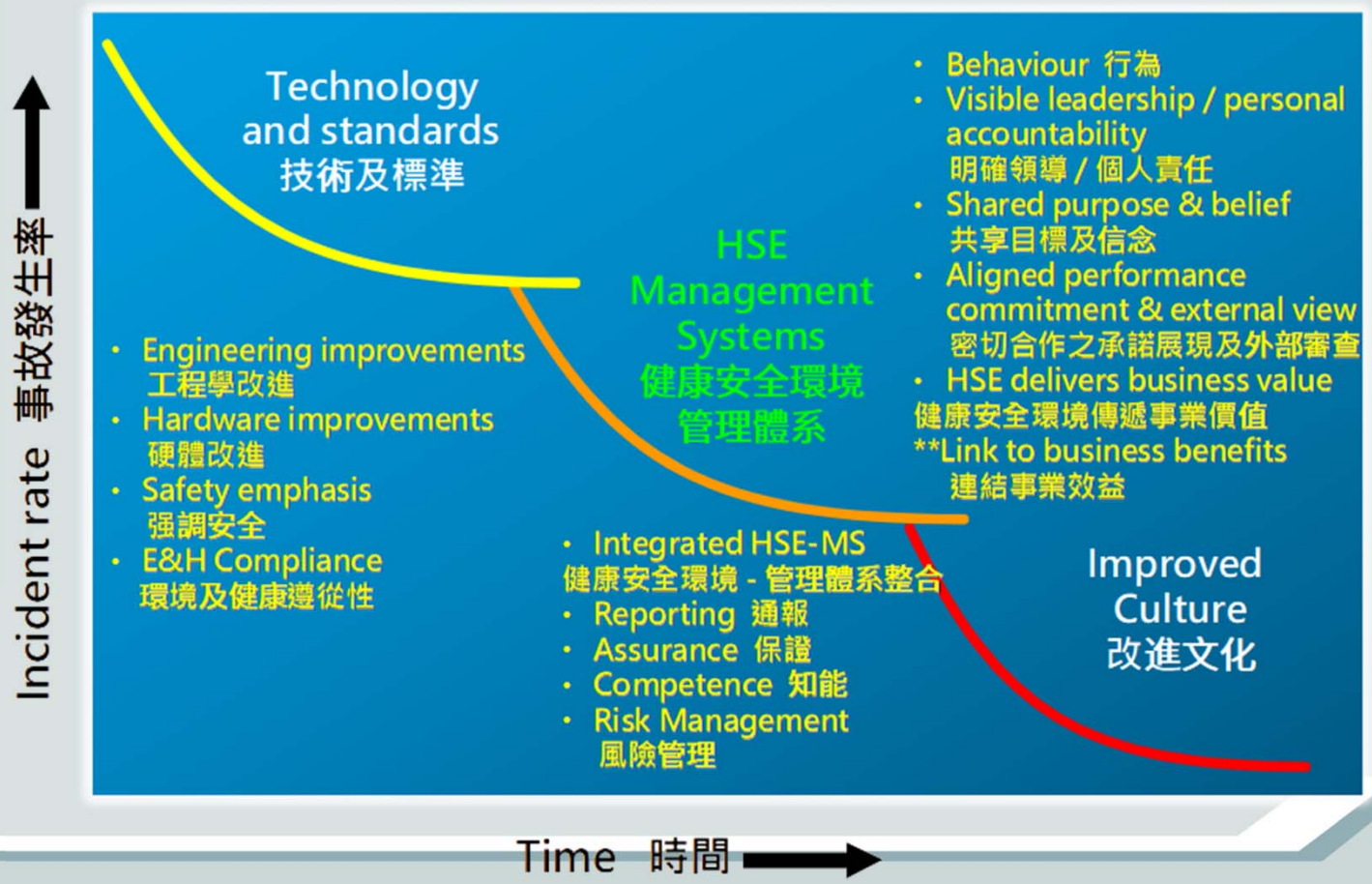


安全文化之發展階段

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建立生物安全文化_2/3

H&S Performance - Plateau Effect(健康安全表現-停滯效應)



建立生物安全文化_3/3



Betsy Allen-Manning | Founder & CEO | Corporate Culture Training Solutions | Leadership Training In Dallas Fort Worth

The Culture Clock: How Long Does It Really Take To Build Company Culture?

Tick-tock. Here's the first statistic for you - according to a study by Deloitte, it takes at least 3-5 years to build a strong and positive company culture. That's right, 3-5 years. This timeline can vary based on the size of the organization, the level of commitment, and the resources available. And it takes more than simply writing a fancy mission statement or having cool Happy Hours to build a strong workplace culture. It's all about building a cohesive set of values, beliefs, behaviors, and experiences that everyone in the organization knows, lives by and helps create. Culture takes time, effort, and patience.

https://www.linkedin.com/pulse/culture-clock-how-long-does-really-take-build-company-allen-manning

總結

- 生物安全文化—知易行難的事業
- 實驗室/生材庫負責人應有認知
  - 關鍵角色
  - 積極參與
  - 社會責任
  - 領導榜樣

No news is good news.



Thank You



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