



# Biosafety Levels and Occupational Exposure Control Banding

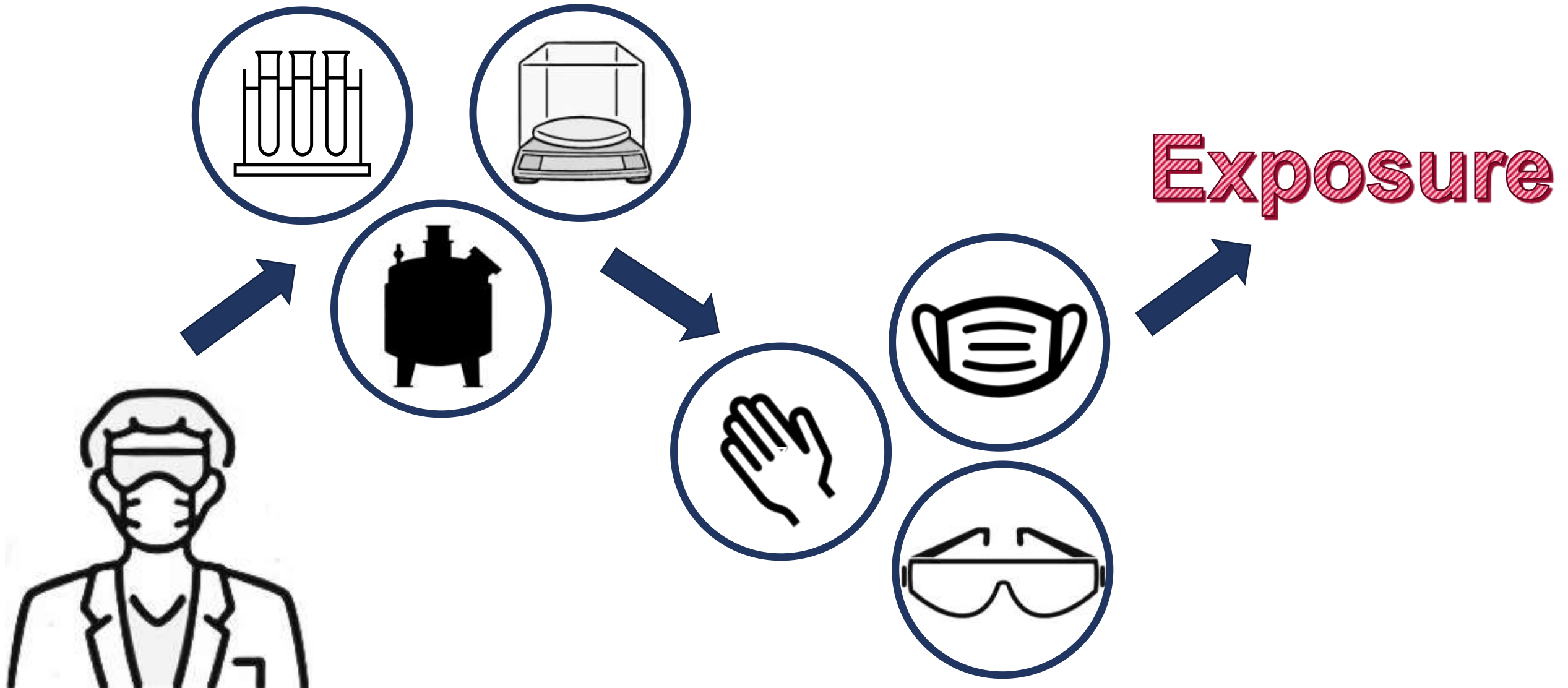
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Gilead Sciences

May 24, 2023



# Pharmaceutical Workplace Exposure



# Hazard Assessment vs. Risk Assessment

## Hazard

### Assessment

- Toxicology
- Potency
- Occupational Exposure Band (OEB) / Occupational Exposure Limit (OEL)
- Biosafety Level (BSL)



Assess workplace exposure



Does potential exposure exceed the OEB / OEL?



## Risk

### Assessment

- IH Data
- Engineering Controls
- Work Practices
- PPE
- Form
- Scale



Reduce exposure potential



# Exposure Control Limits

Data  
Review



$$\frac{\text{Point of Departure (POD)}_{\text{(mg/kg/day)}} \times \text{Body Weight}}{\text{Adjustment/Modifying Factors (F1 x F2 x F3 x F4 x F5 x } \alpha \text{ x } 10 \text{ m}^3)}$$

Limited Data?



Occupational  
Exposure Limit  
(OEL) Derivation

0.2  $\mu\text{g}/\text{m}^3$

5.0  $\text{mg}/\text{m}^3$

10  $\mu\text{g}/\text{m}^3$



# Occupational Exposure Bands



# Occupational Exposure Banding

- Late 1980s/early 1990s: increase in volume of new chemical entities with unknown toxicity and potency
- Development of a “potent compound safety management system”

**Compound Categorization**

**Exposure Control**

**Compound Handling**

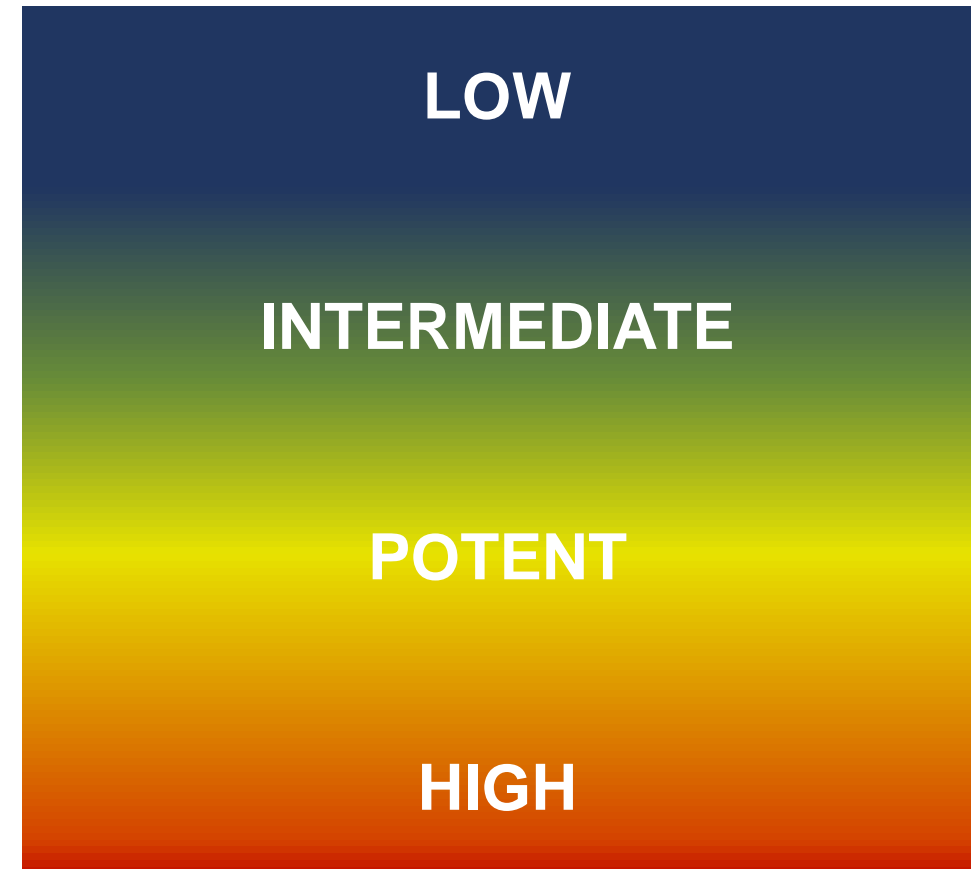


# Compound Categorization

## Data

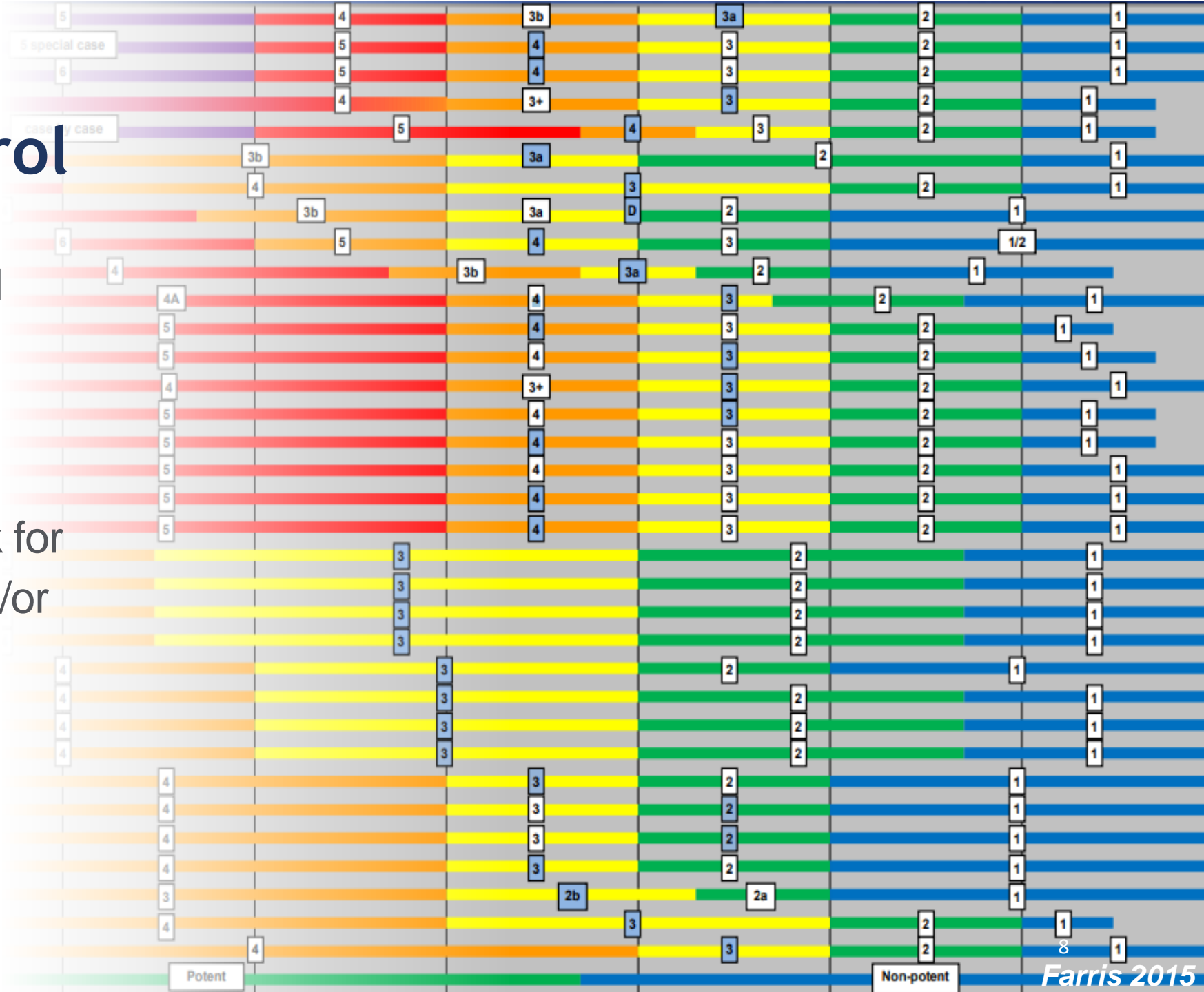
- Mechanism of Action/Target
- Pharmacological Activity
- Anticipated Clinical Dose
- Mutagenicity
- Preclinical and Clinical Data
  - *e.g. Reproductive/Developmental*
- Worker Safety Data
  - *e.g. Skin sensitization*

## Potency



# Exposure Control

- Banding system integrated into organization's engineering controls
- Exposure ranges representing negligible risk for physical, toxicological, and/or pharmacological effect(s)
- Control recommendations based compounds with similar characteristics





# Banding Example - Ader et al. 2005

Band	Potency	Effects	Exposure Limits	Examples
1	Low toxicity	<ul style="list-style-type: none"><li>• Low acute/chronic systemic effects</li><li>• Not a mutagen, reproductive/ developmental toxicant, or carcinogen</li></ul>	> 500 µg/m <sup>3</sup>	Aspirin, naproxen



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2	Intermediate toxicity	<ul style="list-style-type: none"> <li>• Reversible, moderate to high acute systemic toxicity, moderate chronic systemic toxicity (low severity)</li> <li>• Not a mutagen, reproductive/ developmental toxicant, or carcinogen</li> </ul>	10 - 500 µg/m <sup>3</sup>	Insulin, hydrocodone



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3	Potent/toxic	<ul style="list-style-type: none"> <li>• Irreversible, severe acute and chronic systemic effects</li> <li>• Mutagen, reproductive/ developmental toxicant, or carcinogen</li> <li>• Significant pharmacological potency</li> </ul>	0.03 - 10 µg/m <sup>3</sup>	Fentanyl, paclitaxel



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4	Highly potent/ highly toxic	<ul style="list-style-type: none"> <li>Irreversible, severe acute and chronic systemic effects</li> <li>Mutagen, reproductive/ developmental toxicant, or carcinogen</li> <li>Highly potent pharmacological activity</li> </ul>	< 0.03 µg/m <sup>3</sup>	Ethinyl estradiol



# Default Hazard Banding

- Example 'Default' Category – Potent (Category 3)
  - Assumes compound exhibits characteristics of a potent compound
    - Designed to protect for all potential adverse effects



# Biosafety Levels



# Biosafety

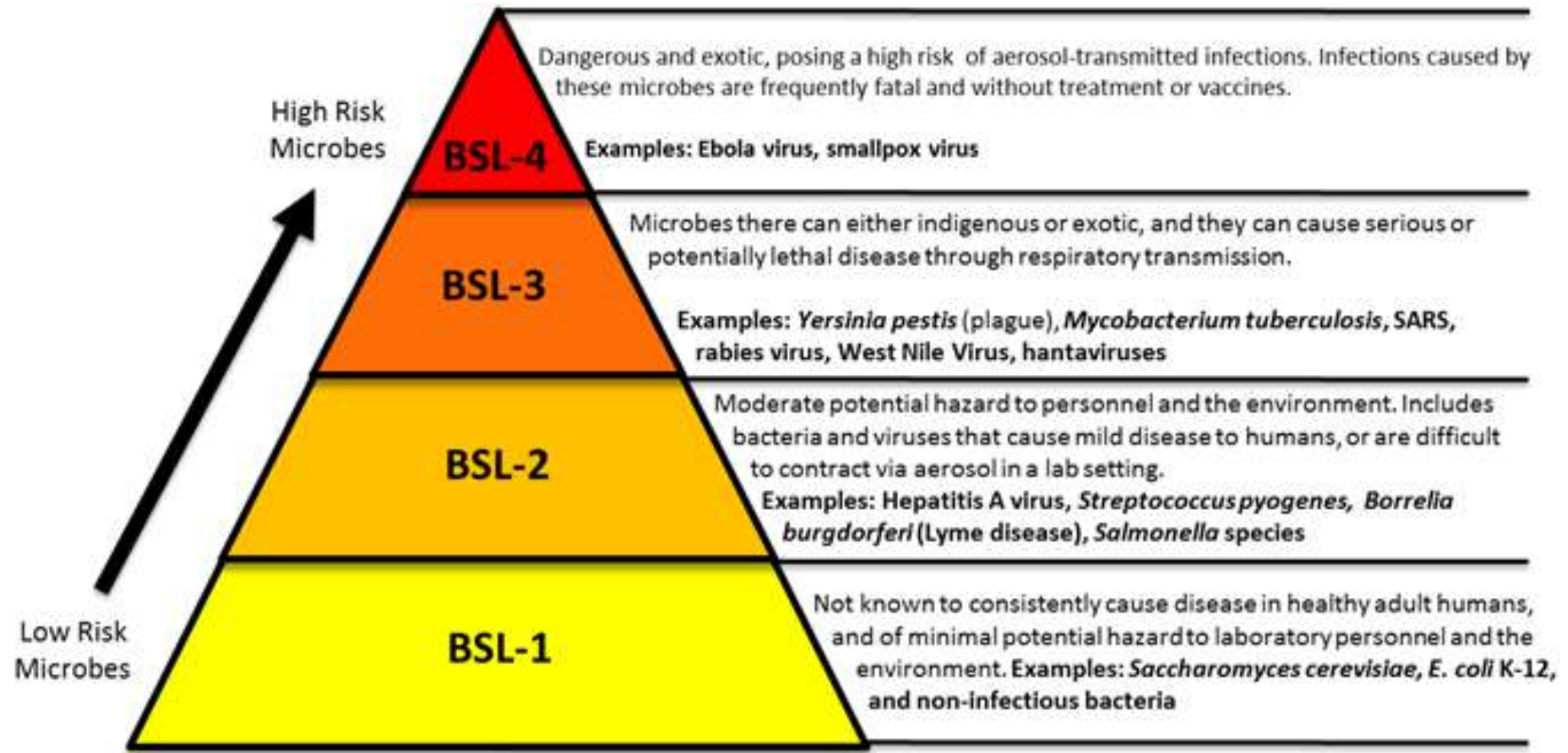
- Safety precautions that reduce risk of exposure to potentially infectious pathogens
- Biocontainment designation system with requirements to protect personnel from potentially harmful pathogenic exposure in research or manufacturing environment
- Risks that determine levels of containment: infectivity, severity of disease, transmissibility, and nature of work conducted



*Centers for Disease Control and Prevention, Graham et al. 2020*



# Biosafety Levels (BSL)

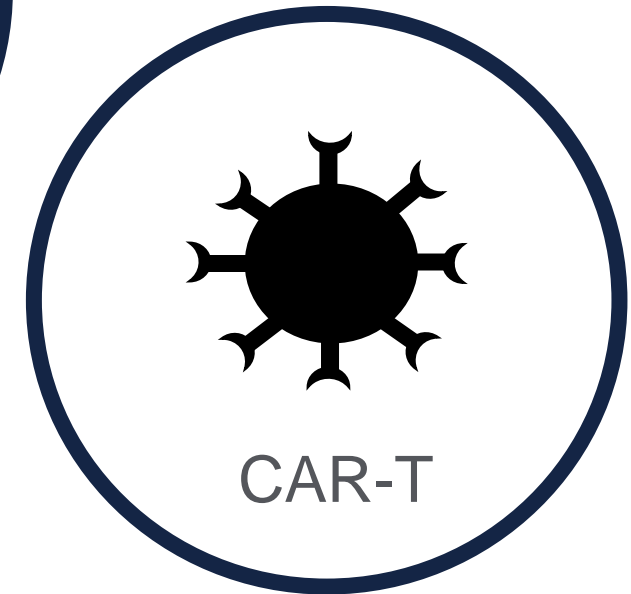
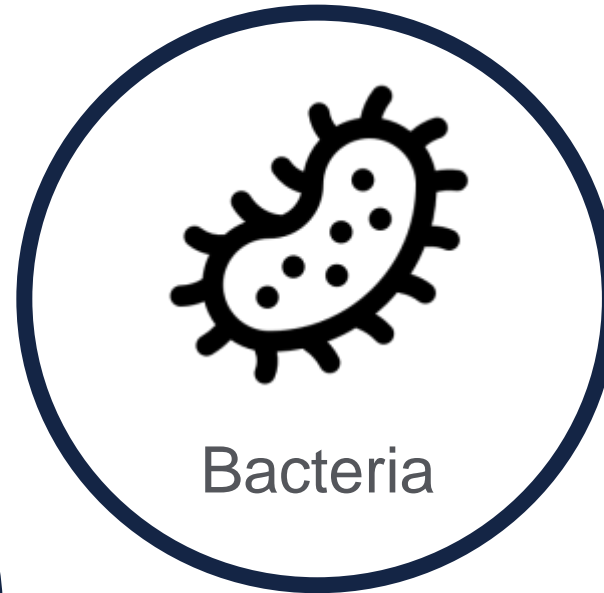
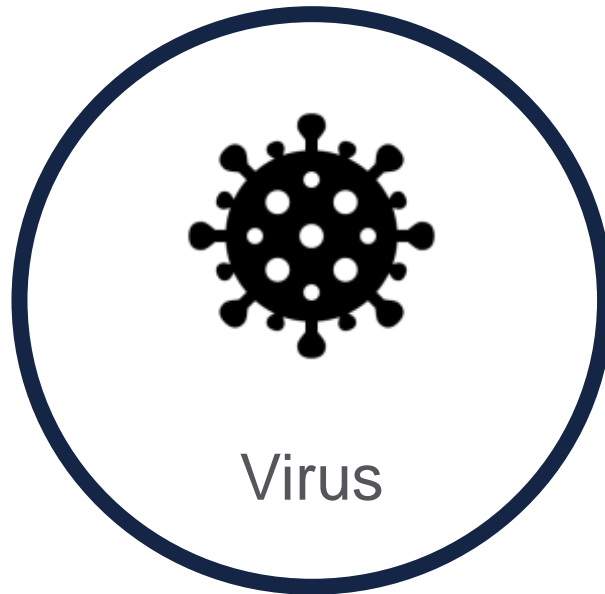
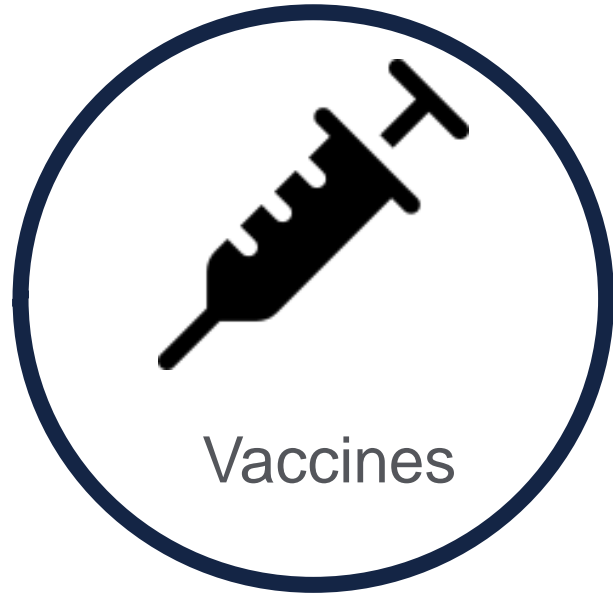


Centers for Disease Control and Prevention





# Pharmaceuticals Examples using BSL Classification



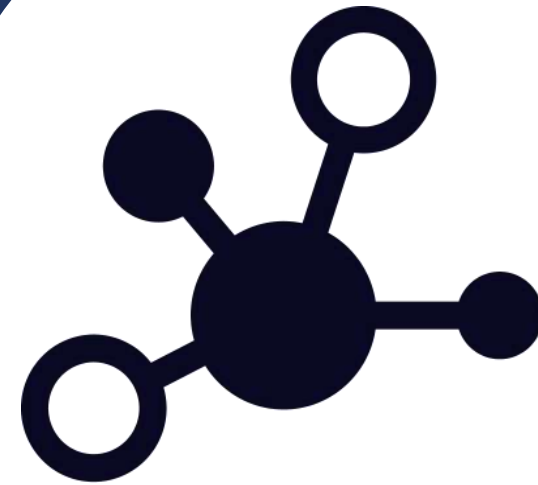
# Biosafety Levels (BSL)

Biosafety Level (BSL)	Definition and Examples
<b>BSL 1</b>	<p>Well-characterized agents not known to consistently cause disease in immunocompetent adult humans; present minimal potential hazard to laboratory personnel and environment.</p> <p>Example: Gene therapy process using a recombinant adeno-associated virus</p>
<b>BSL 2</b>	<p>Moderate-risk agents that cause human disease of varying severity by ingestion or through percutaneous or mucous membrane exposure.</p> <p>Example: Seasonal influenza vaccine from the virus cell bank through virus attenuation; non-replicating viral vaccine vectors</p>
<b>BSL 3</b>	<p>Agents with a known potential for aerosol transmission; agents that may cause serious and potentially lethal infections and that are indigenous or exotic in origin.</p> <p>Example: SARS coronavirus vaccine from the wild type virus</p>
<b>BSL 4</b>	<p>Exotic agents that pose a high individual risk of life-threatening disease by infectious aerosols and for which no treatment is available.</p> <p>Example: Ebola vaccine</p>



# Modalities Impact Classification

- Small molecule (traditional based assessment)
- Biologics (low inhalation bioavailability)
- Antibody Drug Conjugate (high toxicity warhead)
- Vaccines (Biosafety or OEB)
- CAR-T (Biosafety)



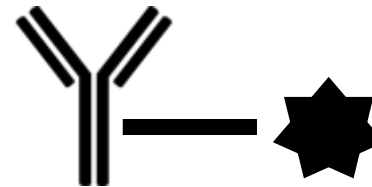
Small Molecule



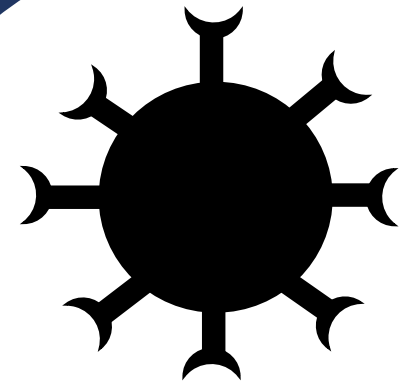
Biologic



Vaccines



ADC



CAR-T

# Summary

- Worker safety based on hazard and risk
- OEB: Assign compounds into bands/categories linked to acceptable exposure ranges and handling practices
- BSL: Biocontainment designation system for handling pathogens
- Therapeutic modality can impact OEB or BSL classification



# References

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- *Centers for Disease Control and Prevention. Recognizing the Biosafety Levels. <https://www.cdc.gov/training/quicklearns/biosafety/>*
- *John P. Farris. (2015) “The Challenge of Working with “Unknowns”: Workplace Evaluation and Control Without Exposure Limits or Monitoring Methods”. SafeBridge Consultants, Inc. California Industrial Hygiene Council.*
- *Jessica C. Graham, Jedd Hillegass, Gene Schulze. (2020) Considerations for Setting Occupational Exposure Limits for Novel Pharmaceutical Modalities. Regulatory Toxicology and Pharmacology. 118*
- *Bruce D. Naumann , Edward V. Sargent , Barry S. Starkman , William J.Fraser , Gail T. Becker & G. David Kirk (1996) Performance-Based Exposure Control Limits for Pharmaceutical Active Ingredients. American Industrial Hygiene Association Journal. 57:1, 33-42*
- *U.S. Department of Health and Human Services Public. Health Service Centers for Disease Control and Prevention. National Institutes of Health. HHS Publication No. (CDC) 21-1112. Revised December 2009.*
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# Thank you

