Analysis of CDC Import Permit Program Inspections from 2013 to 2017

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Centers for Disease Control and Prevention (CDC) Import Permit Program (IPP)

- CDC regulates the importation of infectious biological materials that could cause disease in humans in order to prevent their introduction and spread into the U.S.
  - Infectious biological agents capable of causing illness in humans (e.g., cultures of Zika virus).
    - Also applies for “suspected” select agents when an APHIS/CDC Form 2 is not applicable.
  - Materials known or reasonably expected to contain an infectious biological agent (e.g., blood from nonhuman primates).
  - Vectors of human disease (e.g., live bats, mosquitoes).

https://www.cdc.gov/phpr/ipp/index.htm
**Centers for Disease Control and Prevention (CDC) Import Permit Program (IPP)**

### Most commonly imported agents (2017):

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>1)</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>2)</td>
<td><em>Escherichia coli</em></td>
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<tr>
<td>3)</td>
<td><em>Zika virus</em></td>
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<tr>
<td>4)</td>
<td>Hepatitis c virus</td>
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<tr>
<td>5)</td>
<td>Hepatitis b virus</td>
</tr>
<tr>
<td>6)</td>
<td>Dengue virus</td>
</tr>
<tr>
<td>7)</td>
<td>Cytomegalovirus</td>
</tr>
<tr>
<td>8)</td>
<td><em>Streptococcus</em> species</td>
</tr>
<tr>
<td>9)</td>
<td><em>Salmonella</em> species</td>
</tr>
<tr>
<td>10)</td>
<td><em>Staphylococcus</em> species</td>
</tr>
<tr>
<td>11)</td>
<td>Adenovirus</td>
</tr>
<tr>
<td>12)</td>
<td><em>Klebsiella</em> species</td>
</tr>
<tr>
<td>13)</td>
<td><em>Plasmodium</em> species</td>
</tr>
<tr>
<td>14)</td>
<td><em>Shigella</em> species</td>
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<tr>
<td>15)</td>
<td><em>Enterobacter</em> species</td>
</tr>
<tr>
<td>16)</td>
<td><em>Mycobacterium tuberculosis</em></td>
</tr>
<tr>
<td>17)</td>
<td><em>Campylobacter</em> species</td>
</tr>
<tr>
<td>18)</td>
<td>Epstein-barr virus</td>
</tr>
<tr>
<td>19)</td>
<td><em>Proteus</em> species</td>
</tr>
<tr>
<td>20)</td>
<td><em>Enterococcus</em> species</td>
</tr>
</tbody>
</table>
In 2013, the regulations were amended, 42 CFR 71.54(h)

- Issuance of a permit may be contingent upon an inspection of the importer's facility by the CDC to evaluate whether the importer's biosafety measures (e.g., physical structure and features of the facility, and operational and procedural safeguards) are commensurate with the hazard posed by the infectious biological agent, infectious substance, and/or vector, and the level of risk given its intended use.

https://www.cdc.gov/phpr/ipp/regulations.htm
Scope of CDC Import Permit Inspections

- Verify that biosafety measures are appropriate for the risks of the agent and work.
  - Are the practices and facility conducted in accordance with nationally recognized standards of practice (i.e., Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th edition)?

- Verify the information submitted on the application.
  - Does the applicant have the safety level, primary containment, and personal protective equipment described on the application?
  - Is the work within the scope described on the application?

- Has the permittee complied with the conditions of the permit?

https://www.cdc.gov/phpr/ipp/inspection/index.htm
CDC IPP issues ~2,000 import permits per year and inspects ~40 facilities annually using a risk-based approach.
Risk-Based Inspection Selection Criteria

- Guided by quantitative and objective scoring derived from the application and other sources.
  - Factors include:
    - Risk group(s) of the agent(s) requested
    - Biosafety level(s) reported
    - Culture or propagation activities
    - Work with animals or arthropods
    - History of importation or shipping non-compliance (e.g., CDC Quarantine Stations, U.S. Customs and Border Protection, U.S. Department of Transportation)
    - Registration of laboratories with the Federal Select Agent Program (FSAP)
Some inspections included multiple safety levels.
Import Permit Inspections Conducted: 2013 - 2017

CDC Division of Select Agents and Toxins, Unpublished Data
Biosafety/Containment Findings From Inspections: 2013-2017

- Inspections that require corrective actions = 93%
- Average number of inspection findings = 6.5
  - Deficiencies in biosafety
  - Inaccurate applications
  - Importation without a permit
- Range of inspection findings
  - Minimum = 1
  - Maximum = 33
- 40% of inspections had 3 or fewer observations

Note: Inspection findings can be grouped together if there are multiple deficiencies due to a common observation. Formatted reports may show a lower number of “observations.”
Biosafety/Containment Findings From Inspections: 2013-2017

Top 10 BSL-2 inspection findings:

<table>
<thead>
<tr>
<th>#</th>
<th>BSL-2</th>
<th>Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>72</td>
<td>A9</td>
<td>Laboratory signage</td>
</tr>
<tr>
<td>60</td>
<td>B1</td>
<td>Advising personnel of hazards and entry requirements</td>
</tr>
<tr>
<td>35</td>
<td>A11</td>
<td>Training and information on personal health status</td>
</tr>
<tr>
<td>28</td>
<td>C3</td>
<td>Eye protection and decontamination before reuse</td>
</tr>
<tr>
<td>19</td>
<td>A2</td>
<td>Hand washing</td>
</tr>
<tr>
<td>18</td>
<td>C4b</td>
<td>Remove gloves and hand washing before leaving lab</td>
</tr>
<tr>
<td>18</td>
<td>D1</td>
<td>Self-closing lab doors and locks (according to policies)</td>
</tr>
<tr>
<td>17</td>
<td>C1a</td>
<td>Use of BSC for procedures with aerosol/splash potential</td>
</tr>
<tr>
<td>15</td>
<td>C2</td>
<td>Use of laboratory coats/gowns</td>
</tr>
<tr>
<td>14</td>
<td>A5d</td>
<td>Broken glassware clean up procedures/equipment</td>
</tr>
</tbody>
</table>
Biosafety/Containment Findings From Inspections: 2013-2017

- Top 10 BSL-3 inspection findings:

<table>
<thead>
<tr>
<th>#</th>
<th>BSL-3</th>
<th>Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>A9</td>
<td>Laboratory signage</td>
</tr>
<tr>
<td>47</td>
<td>B1</td>
<td>Advising personnel of hazards and entry requirements</td>
</tr>
<tr>
<td>45</td>
<td>D9</td>
<td>Air flow shall not be reversed under failure conditions</td>
</tr>
<tr>
<td>33</td>
<td>C3</td>
<td>Eye protection and decontamination before reuse</td>
</tr>
<tr>
<td>28</td>
<td>A11</td>
<td>Training and information on personal health status</td>
</tr>
<tr>
<td>24</td>
<td>D15</td>
<td>Documented annual re-verification of BSL3 parameters</td>
</tr>
<tr>
<td>23</td>
<td>D3</td>
<td>Laboratory can be easily cleaned/decontaminated</td>
</tr>
<tr>
<td>22</td>
<td>B10</td>
<td>Use of BSC/physical containment for manipulations</td>
</tr>
<tr>
<td>14</td>
<td>D9a</td>
<td>Visual monitoring device to confirm directional air flow</td>
</tr>
<tr>
<td>13</td>
<td>D2</td>
<td>Hands-free sink for hand washing</td>
</tr>
</tbody>
</table>

https://www.cdc.gov/biosafety/publications/bmbl5/
Biosafety/Containment Findings From Inspections: 2013-Present

- **High impact biosafety inspection findings:**
  - BSL-3 HVAC systems were not functioning properly.
    - A BSL-3 facility was found to be under positive pressure under normal conditions.
  - Spills in centrifuges and potential exposures were not being reported to the laboratory supervisors/biosafety professionals/safety staff.
  - Biological safety cabinets and HEPA filters were out of certification.
    - In some instances, certifications were years out of date.
Application Inaccuracies: 2016 -2017

- Inspections allow for verification of information submitted on an application.
- Applications inspected that were inaccurate = 39%
  - In many cases mistakes or omissions were simple errors.
  - In some cases it appears that applications may have been falsified in attempts to acquire a permit.
Application Inaccuracies: 2013 - Present

- Examples of low or moderate risk:
  - Some laboratory locations (of the same safety level) were not reported in the application.
  - Application reported the use of Powered Air Purifying Respirators (PAPRs), but only N95 respirators were available.
Application Inaccuracies: 2013 - Present

- Examples of high risk:
  - Permittee claimed to have a BSL-3 facility, but only had a BSL-2 facility.
  - Permittee claimed to have a BSL-3 facility, but it had been shut down by the organization after a flood several years prior to the application.
  - Permittee claimed to only conduct *in vitro* work at BSL-2, but conducted work with live mosquitoes at ACL-3.
Importation of Infectious Materials Without a Permit: 2013-Present

- Infectious materials can be intercepted at ports of entry.
- Compliance inspections can occur in response to importations that occur without valid permits.
  - Self-reported by organization.
  - Complaints from a 3rd party.
  - Complaints from federal partners.
- 6 inspections found that materials were imported without a valid CDC import permit.
  - 1 instance was linked to a laboratory associated infection in 2016.
Impact of Inspections: 2013 -Present

- 184 inspections were conducted from 2013 -2017.

- 12 permits were revoked.
  - 10 permittees did not have the biosafety level, containment, or facilities as described in the application for their permit.
  - 2 permittees did not allow inspection of their facility.

- 2 permit applications were voluntarily withdrawn in response to the inspection findings.
  - Permittees were not able meet ABSL-2 or ABSL-3 facility standards.
Impact of Inspections: 2013 - Present

- **2 permit applications were denied.**
  - 1 permittee did not have their ABSL3 facility constructed at the time of the inspection.
  - 1 permittee was suspended by their organization for non-compliance.

- **2 permittees were unable to adequately address all inspection findings after 1 year.**
  - Inspection findings were related to deficiencies in the HVAC of BSL facilities.
  - Both were placed on a watch list to prevent future issuance of permits, until corrective actions can be confirmed.
  - Information is shared with CDC quarantine stations and port of entry staff.
Conclusions

- Most inspections had findings that required corrective action, but 40% of all inspection reports had 3 or fewer observations.
  - Many organizations have strong oversight and biosafety.
- ~10% of inspections resulted in some type of significant action taken (e.g., revocation, denial, watch list).
- A substantial number (39%) of applications/permits inspected contain inaccurate information.
Conclusions

- The 2013 revision to the import regulations has made a positive impact on biosafety and public safety.

- Onsite inspections by CDC benefit some organizations and individual permittees to identify and develop mitigation strategies to reduce overall risk of handling these imported materials.
Next Steps

- The CDC IPP will continue to implement the regulations as revised in 2013 to verify that importers implement appropriate biosafety measures.

- Increasing onsite inspections by CDC will better serve organizations and individual permittees to ensure necessary biosafety measures are in place for handling these imported materials.
Final Note: Release of eIPP

- Released in August 2018
- Addition of BSO contact information

https://eipp.cdc.gov/
Acknowledgements

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Glen DeGruy, Team Lead
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Janet Wilson, Sr. Microbiologist
Discussion

https://www.cdc.gov/phpr/ipp/index.htm
importpermit@cdc.gov or 404-718-2077

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E-mail: cdcinfo@cdc.gov Web: www.cdc.gov

The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention.