Analysis of CDC Import Permit Program Inspections from 2013 to 2017



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Centers for Disease Control and Prevention
Office of Public Health Preparedness and Response

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 non-human primates).
  - Vectors of human disease (e.g., live bats, mosquitoes).

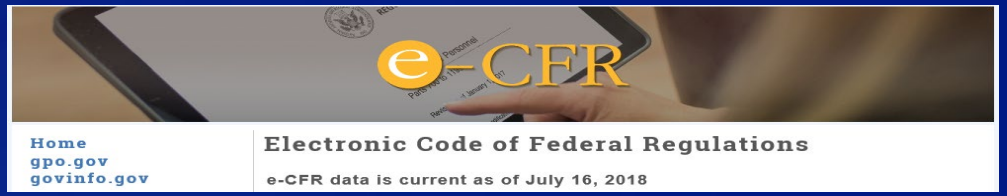
https://www.cdc.gov/phpr/ipp/index.htm

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

Most commonly imported agents (2017):	
1) Human Immunodeficiency Virus	11) Adenovirus
2) *Escherichia coli*	12) *Klebsiella* species
3) Zika virus	13) *Plasmodium* species
4) Hepatitis c virus	14) *Shigella* species
5) Hepatitis b virus	15) *Enterobacter* species
6) Dengue virus	16) *Mycobacterium tuberculosis*
7) Cytomegalovirus	17) *Campylobacter* species
8) *Streptococcus* species	18) Epstein-barr virus
9) *Salmonella* species	19) *Proteus* species
10) *Staphylococcus* species	20) *Enterococcus* species

CDC Import Permit Regulations

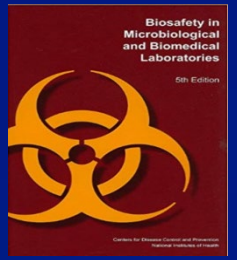
- In 2013, the regulations were amended, 42 CFR 71.54(h)
  - Issuance of a permit may be contingent upon an inspection of the importer's facility by the CDC to evaluate whether the importer's biosafety measures (e.g., physical structure and features of the facility, and operational and procedural safeguards) 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)?

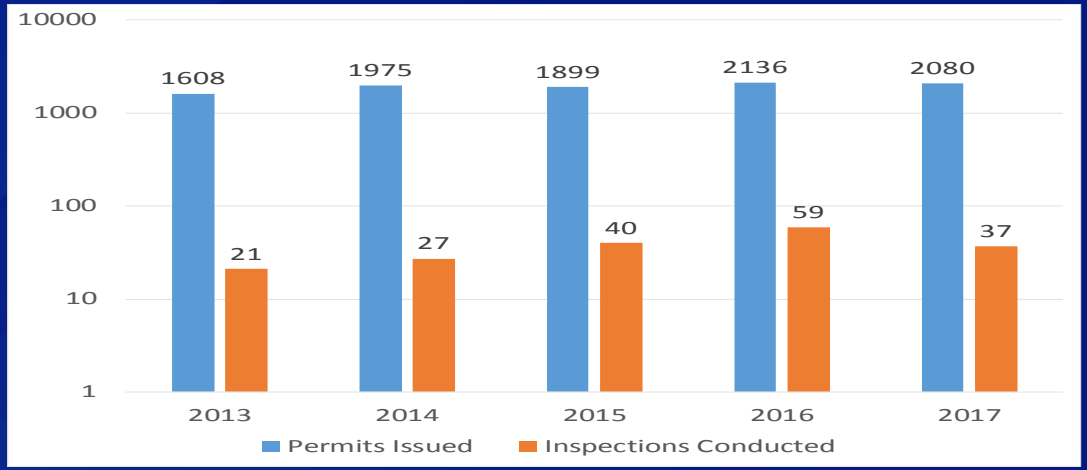


- **Verify the information submitted on the application.**
  - Does the applicant have the safety level, primary containment, and personal protective equipment described on the application?
  - Is the work within the scope described on the application?
- **Has the permittee complied with the conditions of the permit?**

https:// www.cdc.gov/phpr/ipp/inspection/index.htm

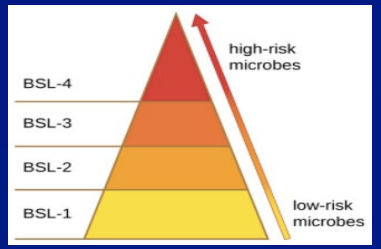
Number of Permits Issued Compared to the Number of Inspections

- CDC IPP issues ~2,000 import permits per year and inspects ~40 facilities annually using a risk -based approach.

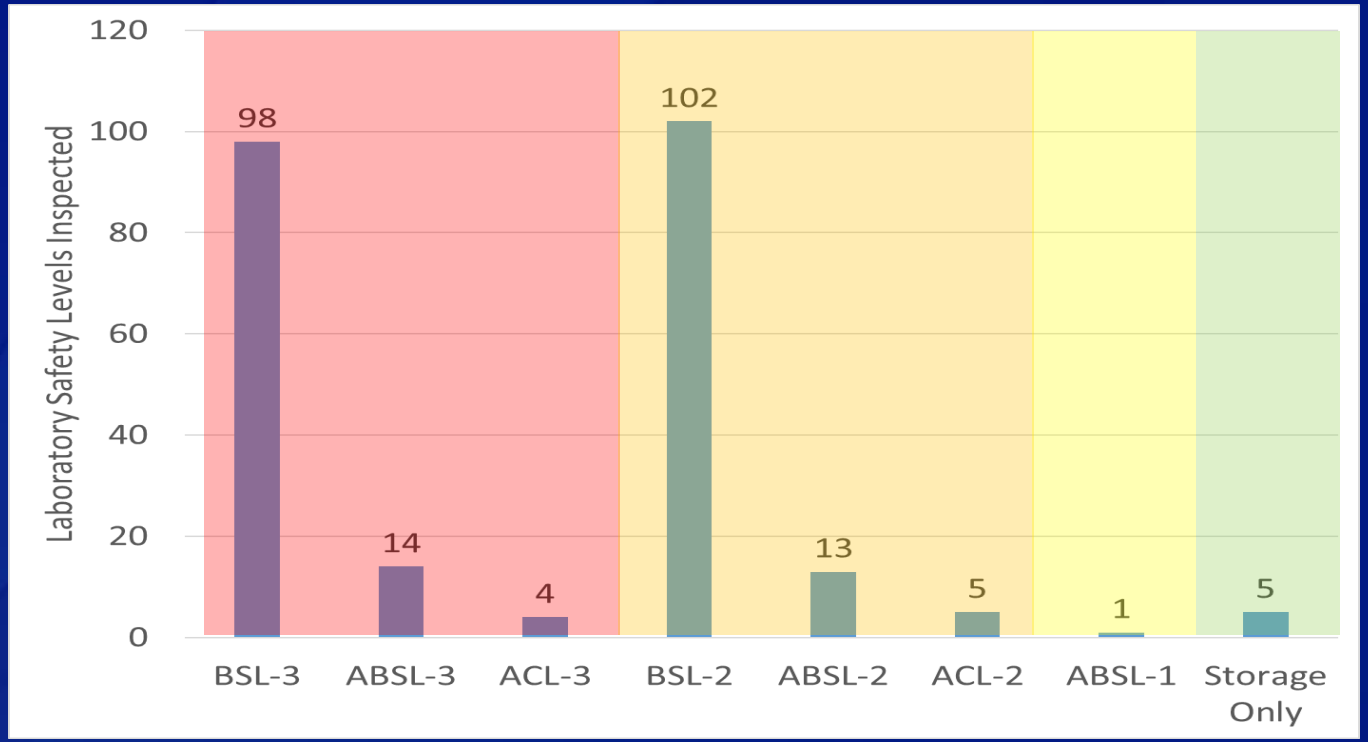


Risk-Based Inspection Selection Criteria

- **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)

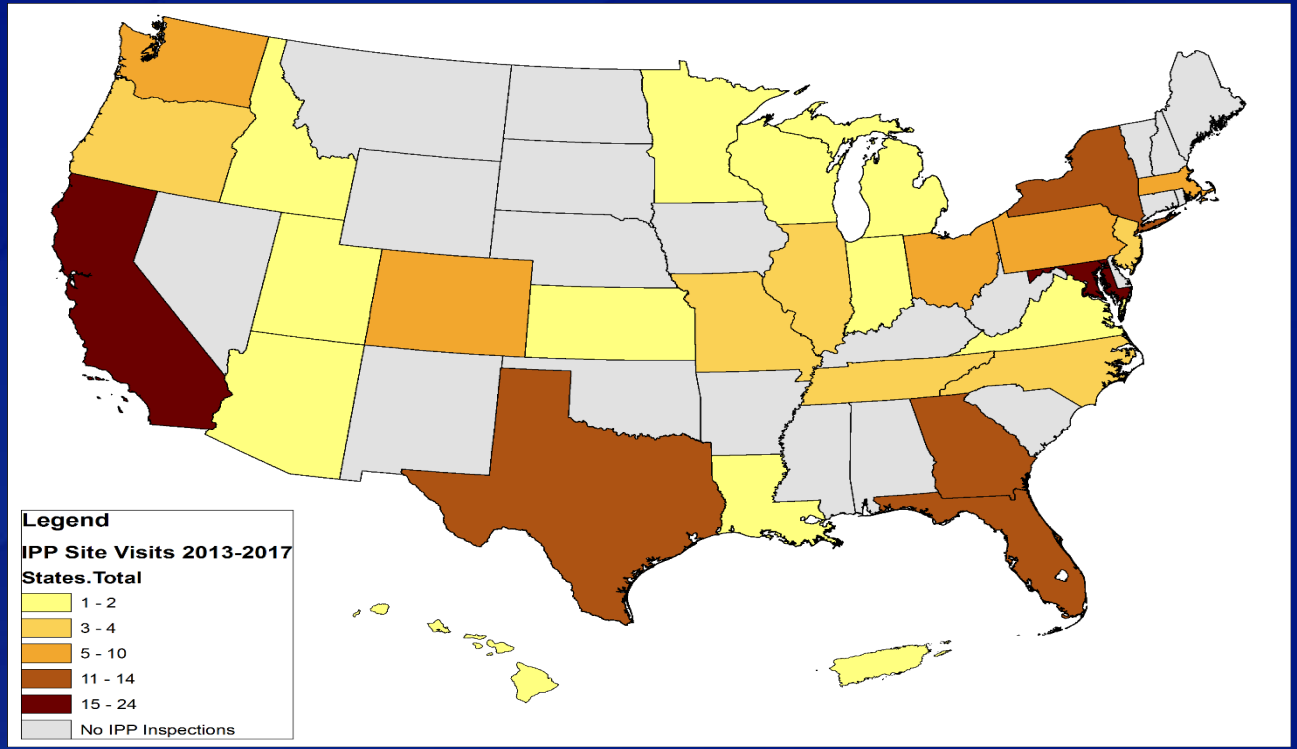


Biosafety Levels Inspected: 2013-2017



Some inspections included multiple safety levels.

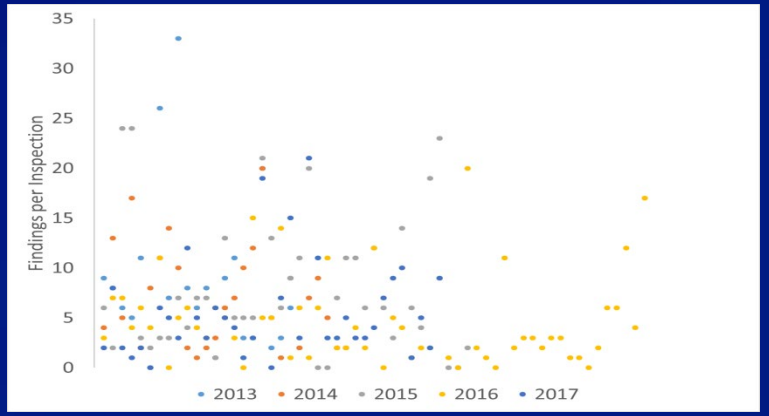
Import Permit Inspections Conducted: 2013 -2017



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:

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

Biosafety/Containment Findings From Inspections: 2013-2017

- Top 10 BSL-3 inspection findings:

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

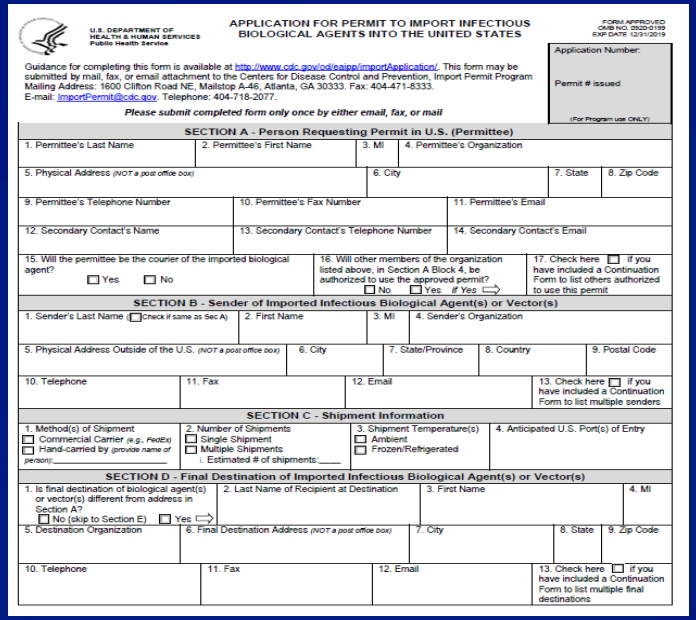
https://www.cdc.gov/biosafety/publications/bmbl5/

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.



U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service

APPLICATION FOR PERMIT TO IMPORT INFECTIOUS BIOLOGICAL AGENTS INTO THE UNITED STATES

FORM APPROVED
OMB NO. 0920-0199
EXP DATE 12/31/2019

Application Number:

Permit # issued

(For Program use ONLY)

Guidance for completing this form is available at http://www.cdc.gov/od/eaipp/importApplication/. This form may be submitted by mail, fax, or email attachment to the Centers for Disease Control and Prevention, Import Permit Program
Mailing Address: 1600 Clifton Road NE, Mailstop A-46, Atlanta, GA 30333. Fax: 404-471-8333.
E-mail: ImportPermit@cdc.gov. Telephone: 404-718-2077.

Please submit completed form only once by either email, fax, or mail

SECTION A - Person Requesting Permit in U.S. (Permittee)

1. Permittee's Last Name	2. Permittee's First Name	3. MI	4. Permittee's Organization
5. Physical Address *(NOT a post office box)*	6. City	7. State	8. Zip Code
9. Permittee's Telephone Number	10. Permittee's Fax Number	11. Permittee's Email	
12. Secondary Contact's Name	13. Secondary Contact's Telephone Number	14. Secondary Contact's Email	
15. Will the permittee be the courier of the imported biological agent? ☐ Yes ☐ No	16. Will other members of the organization listed above, in Section A Block 4, be authorized to use the approved permit? ☐ No ☐ Yes *If Yes* ⇨	17. Check here ☐ if you have included a Continuation Form to list others authorized to use this permit	

SECTION B - Sender of Imported Infectious Biological Agent(s) or Vector(s)

1. Sender's Last Name (☐ Check if same as Sec A)	2. First Name	3. MI	4. Sender's Organization
5. Physical Address Outside of the U.S. *(NOT a post office box)*	6. City	7. State/Province	8. Country	9. Postal Code
10. Telephone	11. Fax	12. Email	13. Check here ☐ if you have included a Continuation Form to list multiple senders

SECTION C - Shipment Information

1. Method(s) of Shipment ☐ Commercial Carrier *(e.g., FedEx)* ☐ Hand-carried by *(provide name of person)*:_____	2. Number of Shipments ☐ Single Shipment ☐ Multiple Shipments ↓ Estimated # of shipments:____	3. Shipment Temperature(s) ☐ Ambient ☐ Frozen/Refrigerated	4. Anticipated U.S. Port(s) of Entry

SECTION D - Final Destination of Imported Infectious Biological Agent(s) or Vector(s)

1. Is final destination of biological agent(s) or vector(s) different from address in Section A? ☐ No (skip to Section E) ☐ Yes ⇨	2. Last Name of Recipient at Destination	3. First Name	4. MI
5. Destination Organization	6. Final Destination Address *(NOT a post office box)*	7. City	8. State	9. Zip Code
10. Telephone	11. Fax	12. Email	13. Check here ☐ if you have included a Continuation Form to list multiple final destinations

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.

4. Scientific name of known/suspected biological agent(s) including Genus and species	5. Strain Designation (list "N/A" if not applicable)	6. Location		7. Laboratory or Storage (Select one or both)		8. Laboratory Safety Level (Leave blank if storage only)	9. Person Responsible for Laboratory
Scientific Name	Strain Designation	Bldg	Suite/Room	Lab	Storage	Safety Level	Responsible Person
a.				☐	☐		
b.				☐	☐		
c.				☐	☐		
d.				☐	☐		

SECTION G - Biosafety Measures

1. Primary Containment to be used *(Check all that apply)*	2. Personal Protective Measures to be used *(Check all that apply)*	3. Personnel Training provided *(Check all that apply)*	4. Has the permittee implemented biosafety measures commensurate with the hazard posed by the infectious biological agent, infectious substance, and/or vector to be imported, and the level of risk given its intended use?
☐ None (open bench) ☐ Class I ☐ Class II, Type _____ ☐ Class III ☐ Fume Hood ☐ Other *(please describe)*:	☐ Gloves ☐ Protective Clothing ☐ Goggles and/or Face Shield ☐ Facemask ☐ Respirators: Type ☐ N95/100 ☐ PAPR ☐ Immunizations ☐ Other *(please describe)*:	☐ Risk(s) associated with the imported biological agent(s) ☐ Hazardous Material Packing/Shipping ☐ Laboratory Standard Practices ☐ Hazardous Waste Handling/Disposal ☐ Emergency Response Procedures ☐ Spill Procedures ☐ Other *(please describe)*:	☐ No ☐ Yes *(Plan may be required to be submitted)*

SECTION D - Final Destination of Imported Infectious Biological Agent(s) or Vector(s)

1. Is final destination of biological agent(s) or vector(s) different from address in Section A? ☐ No (skip to Section E) ☐ Yes ⇨	2. Last Name of Recipient at Destination	3. First Name	4. MI
5. Destination Organization	6. Final Destination Address *(NOT a post office box)*	7. City	8. State / 9. Zip Code
10. Telephone	11. Fax	12. Email	13. Check here ☐ if you have included a Continuation Form to list multiple final destinations

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 ABSL-3 facility constructed at the time of the inspection.
  - 1 permittee was suspended bytheir 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-3 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

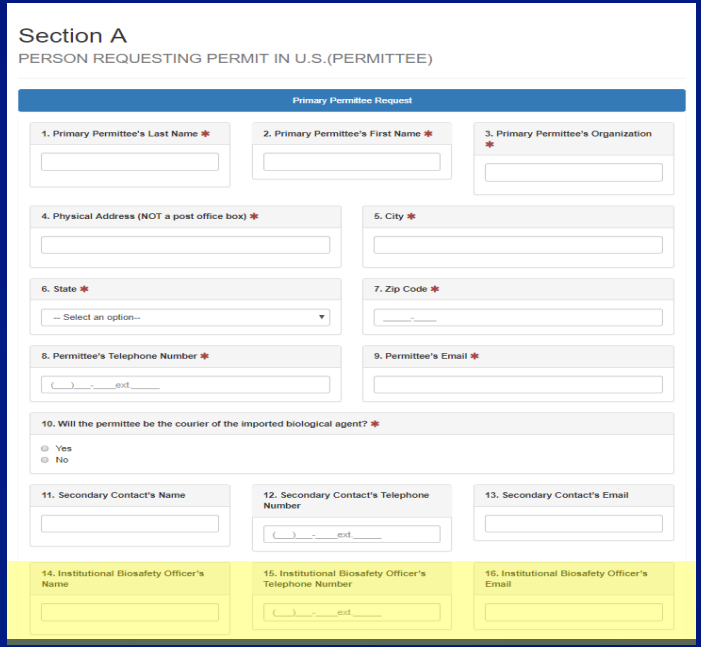
- The CDC IPP will continue to implement the regulations as revised in 2013 to verify that importers implement appropriate biosafety measures.

- 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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Discussion

https://www.cdc.gov/phpr/ipp/index.htm

importpermit@cdc.gov or 404-718-2077




For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333
Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov Web: www.cdc.gov

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