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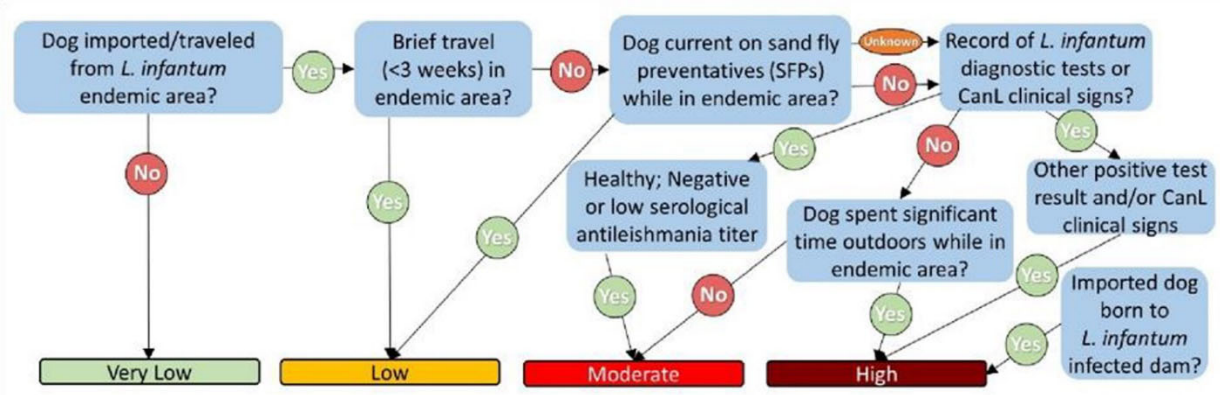
Operational Risk Assessment Tool for Evaluating *Leishmania infantum* Introduction and Establishment in the United States through Dog Importation

Appendix

Operational Risk Assessment Tool

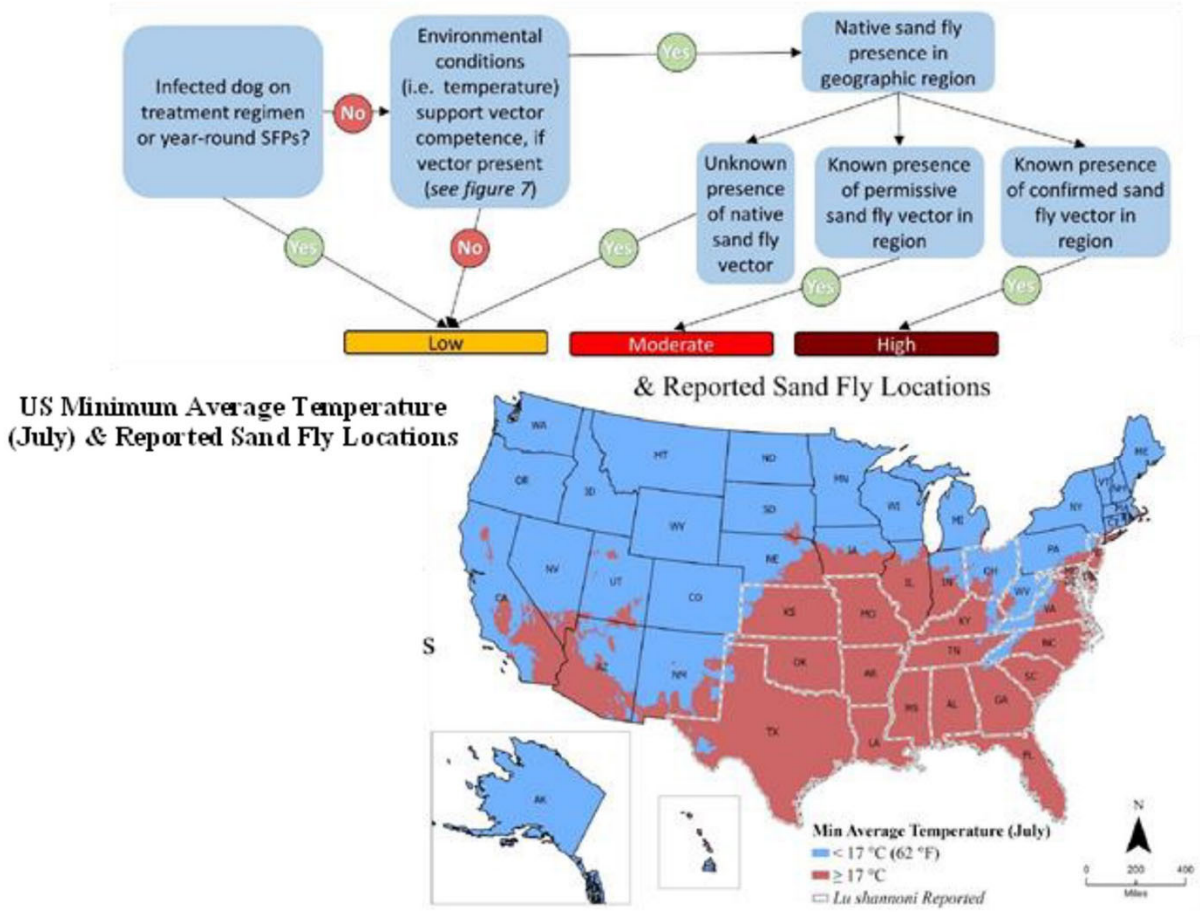
Step 1. Entry assessment: The entry assessment describes biologic pathways needed for US importation of a *L. infantum*-infected dog and estimates the probability of occurrence. Probability is impacted by imported country of origin, sand fly preventative (SFP) use during travel, duration of time spent in endemic country, dog occupation and outdoor exposure to sand flies, clinical progression of infection; *L. infantum*–infected dams (Appendix Figure 1).



Appendix Figure 1. Schematic for determining probability of importing a *Leishmania infantum*–infected dog.

Step 2. Exposure assessment: The exposure assessment describes biologic pathways needed for transmission of *L. infantum* from an infected imported dog and subsequent exposure of humans and other animals in the US, and estimates the probability of occurrence. Probability

is impacted by sand fly preventative (SFP) use during infection, presence of permissible sand fly species, leishmania treatment use during infection, dog occupation and outdoor exposure to sand flies, and weather conditions that affect vector competence (Appendix Figure 2).



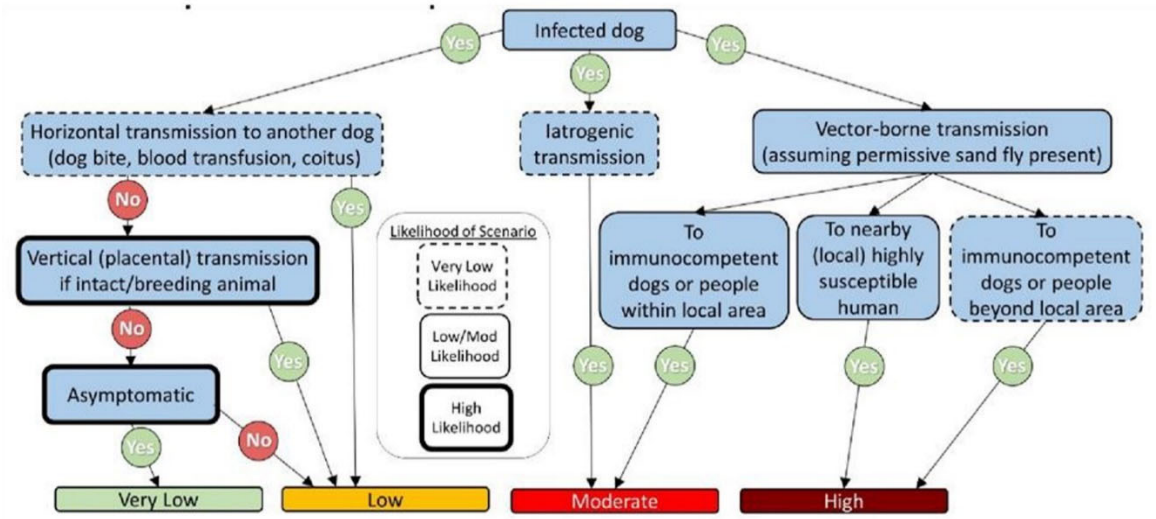
Appendix Figure 2. Schematic for determining probability of vectorborne transmission. Blue areas indicate average temperatures are less likely to support vector competence; red areas indicate average temperatures are more likely to support vector competence; white outline shows states with reported permissive vector species, *Lu. shannoni*.

Step 3. Determine combined probability of events: use the combination probability matrix below to determine conditional probability estimates of *L. infantum* importation via infected dogs followed by vector borne transmission in the US via sand flies (Appendix Figure 3).

Vectored transmission via sand flies	Importation of *L. infantum*-infected dogs			
	Very Low	Low	Moderate	High
Low	Very Low	Low	Low	Low
Moderate	Low	Low	Moderate	Moderate
High	Low	Moderate	Moderate	High

Appendix Figure 3. Combination probability matrix for determining conditional probability estimates of *L. infantum* importation via infected dogs after vectorborne transmission via sand flies in the United States.

Step 4. Consequence assessment: The consequence assessment describes the impact on human and dog health if *L. infantum* is established in the general US dog population (Appendix Figure 4). After considering the likelihood of potential scenarios, the impact can be estimated.



Appendix Figure 4. Consequence assessment for effects on human and dog health if *L. infantum* is established in the general U.S. dog population.

Step 5. Estimate final risk: use the final risk estimation matrix below to determine the *L. infantum* importation risk in dogs from endemic countries based on likelihood of importation and vector borne transmission and its consequences on human and dog health (Appendix Figure 5).

Combined importation & transmission probability	Impact of *L. infantum* transmission on dog and human health			
	Very Low	Low	Moderate	High
Very Low	Negligible Risk	Negligible Risk	Very Low Risk	Low Risk
Low	Negligible Risk	Very Low Risk	Low Risk	Moderate Risk
Moderate	Very Low Risk	Low Risk	Moderate Risk	High Risk
High	Very Low Risk	Low Risk	Moderate Risk	High Risk

Appendix Figure 5. Risk estimation matrix or determining the *L. infantum* importation risk in dogs from endemic countries based on likelihood of importation and vectorborne transmission and its consequences on human and dog health.

A complete reference guide to the risk assessment tool is provided on the last 2 pages of this appendix.

Case Study Examples

Case 1

A 10-year-old intact female spaniel dog that was adopted in Spain is moving to Georgia. The dog's current veterinarian reports that there are no open skin lesions, but the dog did have a mass on the leg that was biopsied and revealed *Leishmania*. The dog was tested via quantitative serology and is seropositive at a titer 2-fold higher than the laboratory's established cutoff. The dog is intended to be used as a breeding animal and has not been maintained on sand fly preventatives (SFPs).

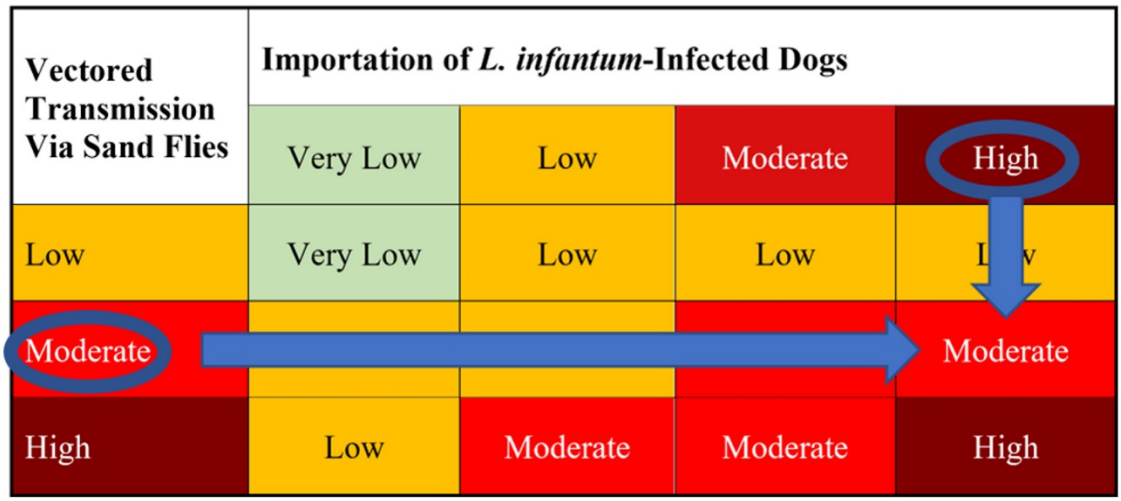
Risk Assessment

Step 1 – Determine probability of importing an infected dog: high. This dog originated from an endemic country, is symptomatic for leishmaniosis, and the diagnosis was confirmed by serology and histopathology.

Step 2 – Determine probability of vector-borne transmission in the US: moderate. *Lutzomyia shannoni*, a suspected but unconfirmed vector of *Leishmania infantum* is present in Georgia.

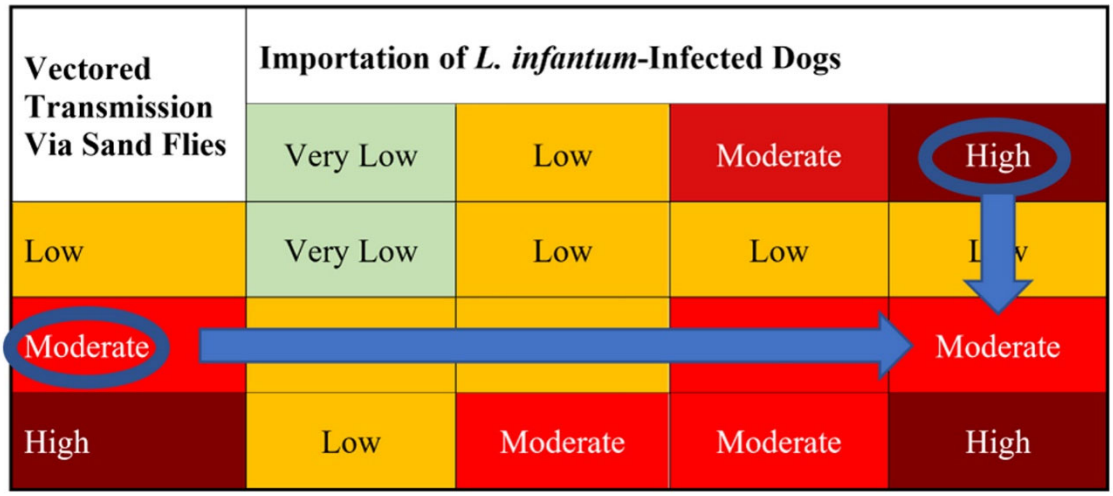
This dog has not previously been maintained on sand fly preventatives.

Step 3 – Determine combined probability of events: moderate. The importation probability for this dog is high while the probability of vector-borne transmission in the US is moderate, thus the combined probability of events using the table in step 3 is moderate (Appendix Figure 6).



Appendix Figure 6. Combined probability matrix for release and exposure assessments for case 1.

Step 4 – Determine the impact on individual canine/human health (Appendix Figure 7).



Appendix Figure 7. Final risk estimation matrix for evaluating the introduction and establishment of *L. infantum* in the United States through dog importation case 1.

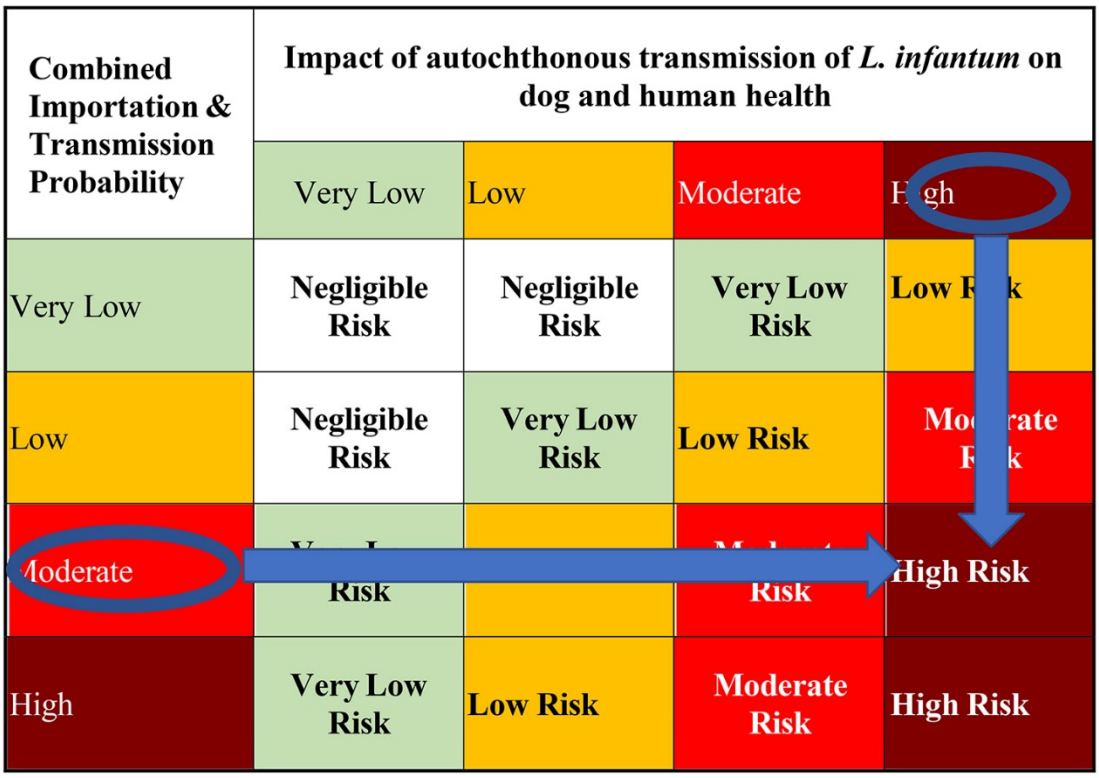
• Step 4a: Horizontal/vertical transmission: This dog was intended to be used as a breeding animal, so the probability of horizontal and vertical transmission is high (the dark circle around vertical transmission on the left side of the diagram) and the impact is low.

• Step 4b: Zoonotic transmission: The dog is symptomatic and confirmed infected, but the probability of direct zoonotic transmission is considered very low (the dotted line circle around zoonotic transmission in the middle arm of the diagram), however the owner is immunocompromised. The impact is considered moderate.

• Step 4c: Vector-borne transmission: The probability of vector-borne transmission is moderate but given that the owner is immunocompromised the impact to the nearby susceptible human population is considered high.

• Step 4d: Select the greatest impact from steps 4a-4c for inclusion in step 5. The greatest of the potential impacts on canine and human health was high (from step 4c).

Step 5 – Determine the final risk estimate. From step 3 the combined probability of events was moderate. Taking all potential event probabilities and potential impacts together, the impact to canine and human health would be considered high (Appendix Figure 8). From the table in step 5, the final risk estimate is high.



Combined Importation & Transmission Probability	Impact of autochthonous transmission of *L. infantum* on dog and human health			
	Very Low	Low	Moderate	High
Very Low	Negligible Risk	Negligible Risk	Very Low Risk	Low Risk
Low	Negligible Risk	Very Low Risk	Low Risk	Moderate Risk
Moderate	Low Risk	Low Risk	Moderate Risk	High Risk
High	Very Low Risk	Low Risk	Moderate Risk	High Risk

Appendix Figure 8. Final estimation matrix for evaluating the introduction and establishment of *L. infantum* in the United States through dog importation from case 1.

Mitigation Strategies and Public Health Response

Always check and comply with any state/local regulations regarding the disposition of dogs with leishmaniosis. In the absence of state/local regulations that would prohibit the dog from entry into the state, animal/public health officials should consider contacting both the owner and the receiving veterinarian.

• Owner – counsel on appropriate prevention methods, e.g., reduce time spent outside during peak sandfly activity and ensure the dog is being maintained on appropriate SFPs to prevent sand fly bites. If authority exists, consider requiring the animal to be sterilized; otherwise advise owner to prohibit animal from breeding. Counsel owner on potential for horizontal transmission to other dogs and zoonotic transmission to people. Because the owner is immunocompromised, they should take extra precautions when handling the dog (e.g., avoiding contact with open wounds and washing hands immediately after handling the dog).

• Veterinarian – determine if treatment is a possibility (as appropriate treatment may reduce a dog's infectiousness); however, treatment is not a requirement as it rarely provides cure

and infected dogs can be managed safely otherwise. Discuss importance of appropriate SFP use and education for owner. Ensure veterinary staff are aware of possibility of iatrogenic transmission through needlesticks and take appropriate precautions. Ensure dog is not used for blood donation.

Case 2

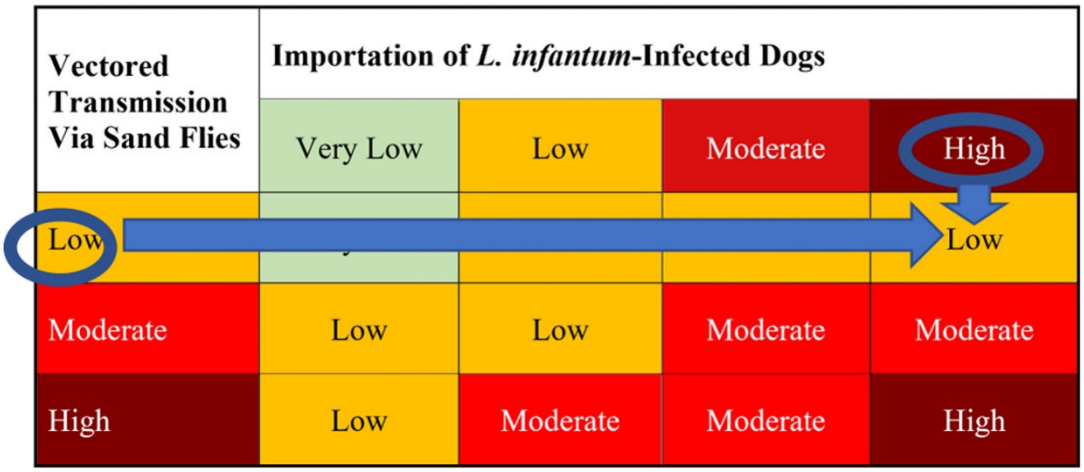
A rescue organization located in Seattle, Washington wants to import a 3 year old intact male shepherd dog from Turkey. The dog was a stray, has no known clinical history, but is reportedly healthy. The dog was tested for leishmaniosis in Turkey by quantitative serology and the results are positive at the cutoff value established by the laboratory. The rescue organization requires that dogs be sterilized before placing them in homes and only adopts to people living in Washington and Oregon.

Risk Assessment

Step 1 – Determine probability of importing an infected dog: high. This dog originated from an endemic country, has unknown clinical history, and unknown use of sand fly preventatives. Testing for leishmaniosis indicates the dog may be infected, but the titer is low.

Step 2 – Determine probability of vector-borne transmission in the US: low. Although the dog has likely not been maintained on appropriate sand fly preventatives, suspected permissive sand fly vectors are not present in Washington or Oregon (where the dog might be placed).

Step 3 – Determine combined probability of events: low. The importation probability for this dog is high while the probability of vector-borne transmission in the US is low, thus the combined probability of events using the table in step 3 is low (Appendix Figure 9).



Appendix Figure 9. Combined probability matrix for release and exposure assessments from case 2.

Step 4 – Determine the impact on individual canine/human health.

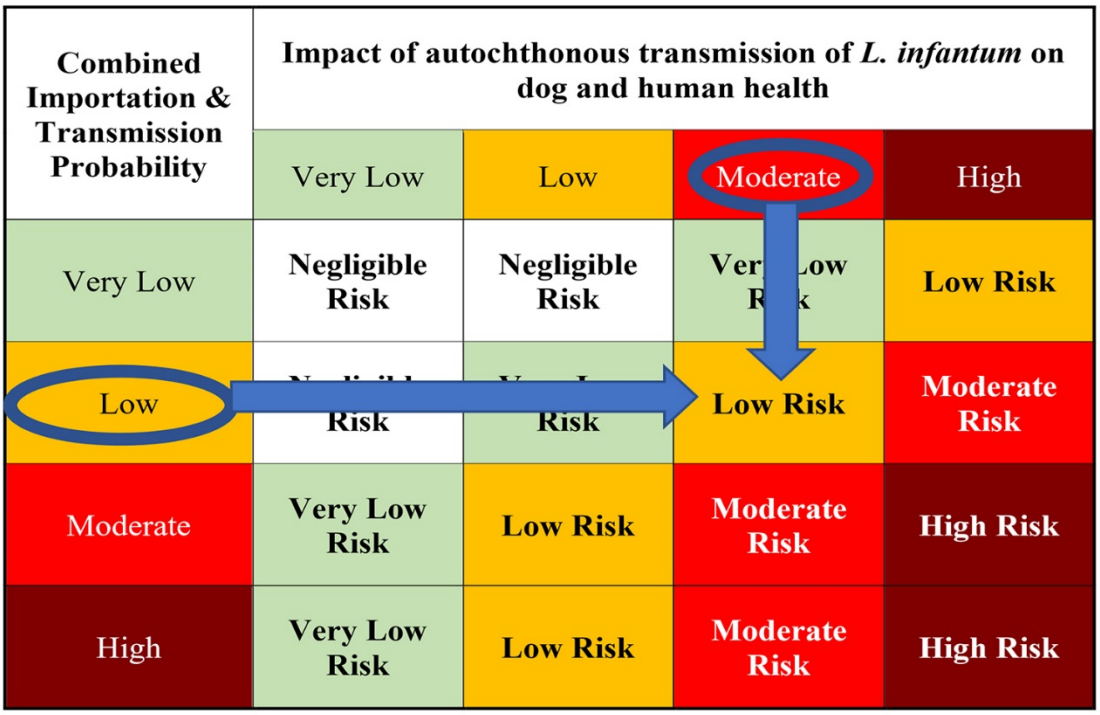
• Step 4a: Horizontal/vertical transmission: The probability of horizontal transmission is low but is dependent on whether the dog will be placed with other dogs. The probability of vertical transmission is negligible since the dog will be sterilized before being rehomed. The dog is also asymptomatic. The overall impact in this scenario is considered very low (if not housed with other dogs) to low.

• Step 4b: Zoonotic transmission: The dog is asymptomatic but likely infected based on quantitative serologic results. The probability of direct zoonotic transmission is considered very low (the dotted line circle around zoonotic transmission in the middle arm of the diagram). The impact is considered moderate.

• Step 4c: Vector-borne transmission: The probability of vector-borne transmission is low as potentially permissive sand fly vectors are not present in the area.

• Step 4d: Select the greatest impact from steps 4a-4c for inclusion in step 5. The greatest of the potential impacts on canine and human health was moderate (from step 4b).

Step 5 – Determine the final risk estimate. From step 3 the combined probability of events was low. Taking all potential event probabilities and potential impacts together, (step 4) the impact to canine and human health would be considered moderate. From the table in step 5, the final risk estimate is low (Appendix Figure 10).



Appendix Figure 10. Final risk estimation matrix for evaluating the introduction and establishment of *L. infantum* in the United States through dog importation from case 2.

Mitigation Strategies and Public Health Response

Always check and comply with any state/local regulations regarding the disposition of dogs with leishmaniosis. In this scenario, the rescue organization should be informed of the overall risk assessment and consider it during the adoption process. Potential adoptees of this dog should be informed of the risk assessment results and educated about leishmaniosis; adoptees with immunocompromised family members or who may come into contact with immunocompromised persons should be informed of the potential risks of zoonotic transmission and advised accordingly. Recommend recheck exam and serology in 6 months and consider sand fly preventives.

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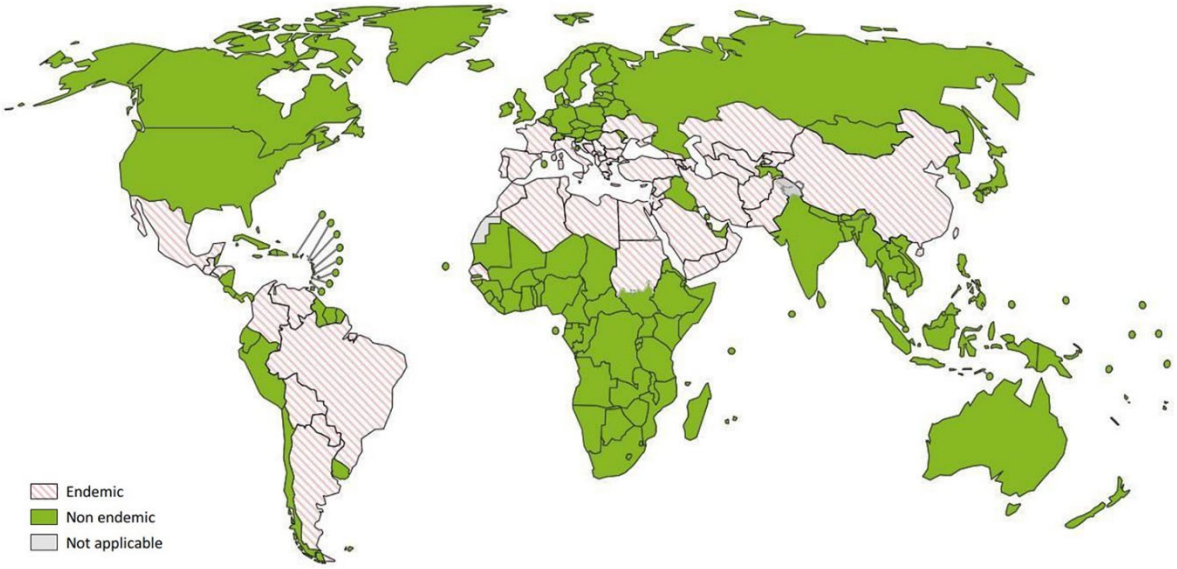


Appendix Figure 11. Map of *Leishmania infantum*–endemic countries. High burden country (*149*). Map and table reproduced from the World Health Organization WHO (*150*), by permission.

New World	
Argentina	Honduras
Bolivia	Mexico
Brazil†	Nicaragua
Columbia	**Paraguay**†
Costa Rica	Venezuela
El Salvador	
Guatemala	

Old World			
Afghanistan	**China**†	Greece	Kyrgyzstan
Albania	Croatia	Iran	Lebanon
Algeria	Cyprus	Iraq	Libyan Aral Jamahiriya
Armenia	Egypt	Israel	Macedonia
Azerbaijan	France	Italy	Malta
Bosnia and Herzegovina	Gambia	Jordan	Mauritania
Bulgaria	**Georgia**†	Kazakhstan	Monaco

Appendix Figure 12. Distribution of *Leishmania infantum* by country or territory, 2009. †High burden country (*149*). Map and table reproduced from the World Health Organization WHO (*150*), by permission.

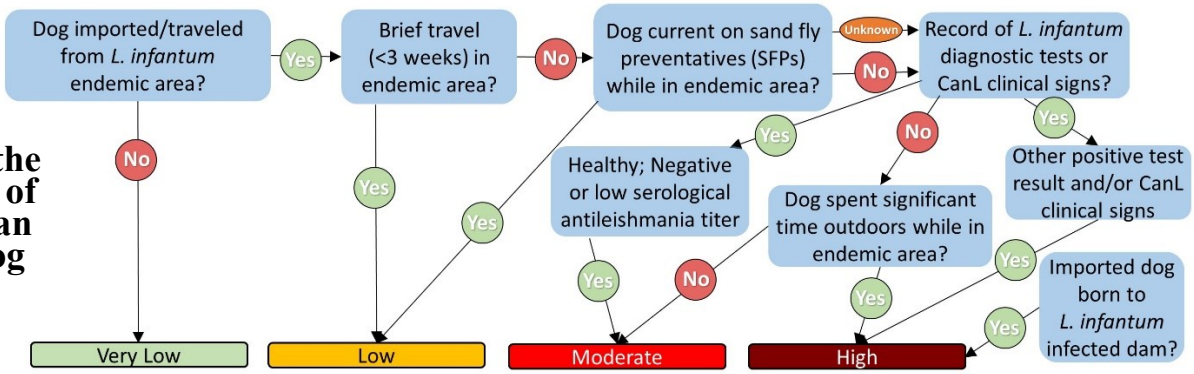
Operational Risk Assessment Tool

Title: Evaluating *Leishmania infantum* risk in the United States through Dog Importation
Purpose: Provide a qualitative tool to assess risks of importing dogs with *L. infantum* into the US

Step 1. Entry assessment: The entry assessment describes biological pathways needed for US importation of a *L. infantum*-infected dog and estimates the probability of occurrence. Probability impacted by:

- Imported country of origin
- Duration of time spent in endemic country
- Clinical progression of infection
- Sand fly preventative (SFP) use during travel
- Dog occupation & outdoor exposure to sand flies
- *L. infantum*-infected dams

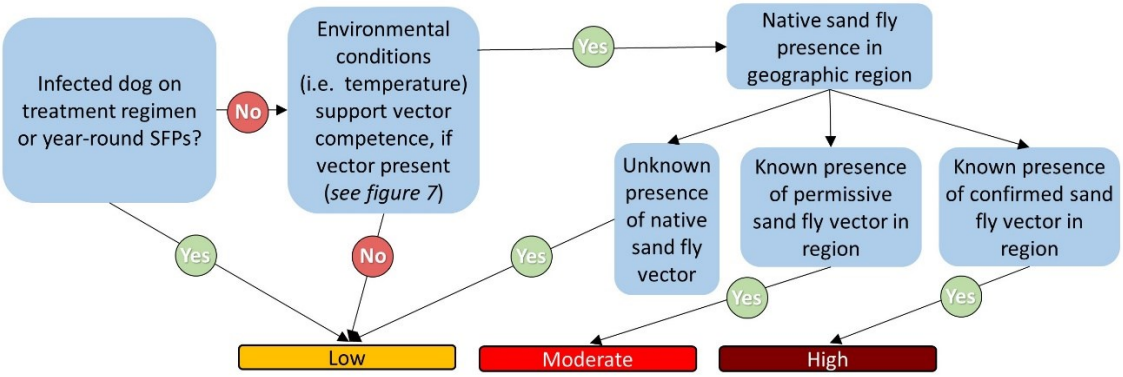
Determine the probability of importing an infected dog



Step 2. Exposure assessment: The exposure assessment describes biological pathways needed for transmission of *L. infantum* from an infected imported dog and subsequent exposure of humans and other animals in the US, and estimates the probability of occurrence. Probability impacting by:

- Sand fly preventative (SFP) use during infection
- Anti-leishmanial treatment use during infection
- Weather conditions that affect vector competence
- Presence of permissible sand fly species
- Dog occupation & outdoor exposure to sand flies

Determine the probability of vector-borne transmission

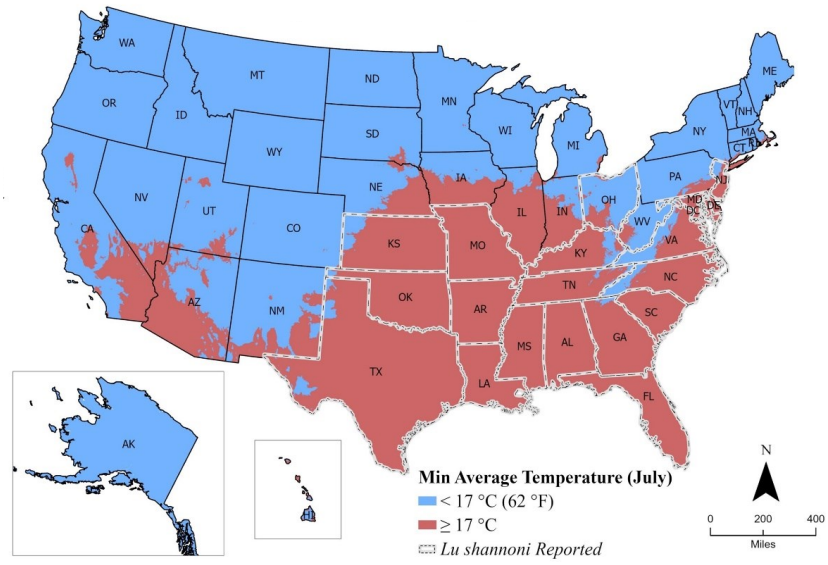


US Minimum Average Temperature (July) & Reported Sand Fly Locations

Blue areas —Average temps are less likely to support vector competence

Red areas—Average temps are more likely to support vector competence

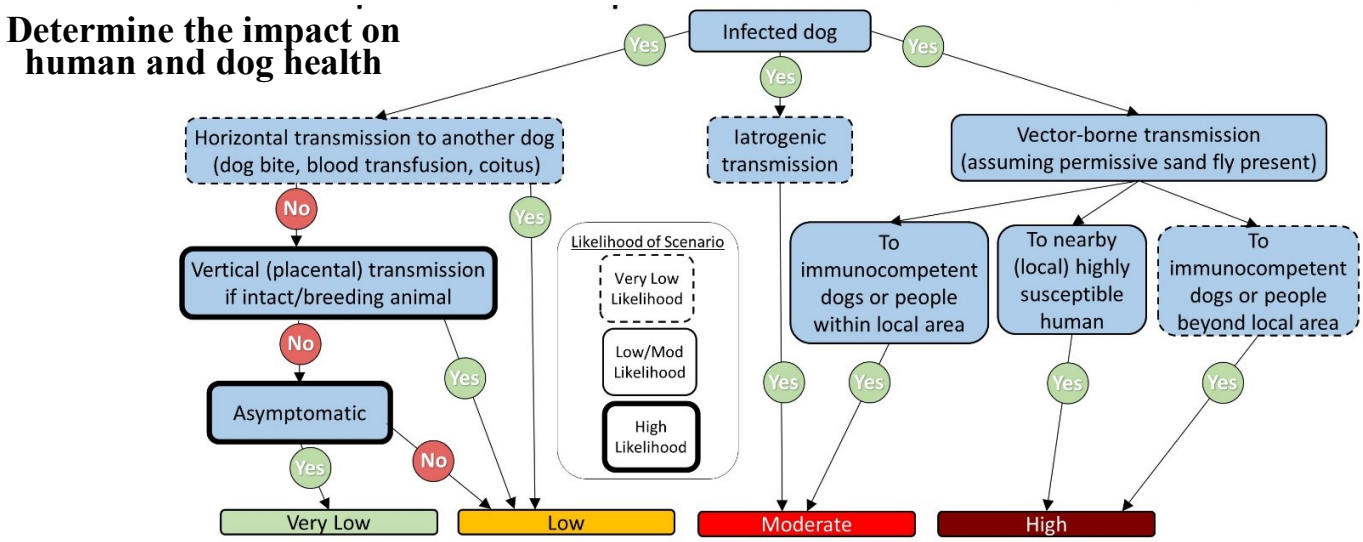
White outline shows states with reported permissive vector (*Lu. shannoni*)



Step 3. Determine combined probability of events: use the combination probability matrix below to determine conditional probability estimates of *L. infantum* importation via infected dogs followed by vector borne transmission in the US via sand flies.

Vectored transmission via sand flies	**Importation of *L. infantum*-infected dogs**			
	Very Low	Low	Moderate	High
Low	Very Low	Low	Low	Low
Moderate	Low	Low	Moderate	Moderate
High	Low	Moderate	Moderate	High

Step 4. Consequence assessment: The consequence assessment describes the impact on human and dog health if *L. infantum* is established in the general US dog population. After considering the likelihood of potential scenarios, the impact can be estimated:



Step 5. Estimate final risk: use the final risk estimation matrix below to determine the *L. infantum* importation risk in dogs from endemic countries based on likelihood of importation and vector borne transmission and it's consequences on human and dog health.

Combined importation & transmission probability	**Impact of *L. infantum* transmission on dog and human health**			
	Very Low	Low	Moderate	High
Very Low	**Negligible Risk**	**Negligible Risk**	**Very Low Risk**	**Low Risk**
Low	**Negligible Risk**	**Very Low Risk**	**Low Risk**	**Moderate Risk**
Moderate	**Very Low Risk**	**Low Risk**	**Moderate Risk**	**High Risk**
High	**Very Low Risk**	**Low Risk**	**Moderate Risk**	**High Risk**