Full application for an addition of a test categories in the EDL

Survey response 1

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41

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1

Start language
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1. Name of test category

Name of the test category addressed in the original submission:
Direct Agglutination Test

2. Pre-submission information

Please indicate your pre-submission response ID: [Pre-submission ID]
263

3. Applicant’s information (primary contact person):

Contact person, name and information of the person submitting the application: [LAST NAME, First name]
RUIZ POSTIGO, Jose Antonio

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postigoj@who.int

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Leishmaniasis COntrol Programme, Department of control of Neglected Tropical Diseases, WHO-HQ

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5. Details of the organization making the submission (if applicable)

Name of the organization making the submission (if applicable): [Name of the organisation]
World Health Organization

Name of the organization making the submission (if applicable): [Address]
Avenue Appia, 20, CH-1211 Geneva 27, Switzerland

Name of the organization making the submission (if applicable): [Department]
Neglected Tropical Diseases

Name of the organization making the submission (if applicable): [Website]
www.who.int

Name of the organization making the submission (if applicable): [Phone number]

6. Details of the organizations supporting the application:

Please provide up to three organizations supporting your application including a. Organization name, b. Contact person, c. Email address:

7. Public health impact of the disease/condition:

Please detail the public health relevance of conditions addressed with the proposed test and add references:

Visceral leishmaniasis is a life threatening parasitic vector-borne disease caused by the obligate intracellular protozoan, Leishmania. It is transmitted by the bites of female phlebotomine sand flies (Herwaldt 1999). Leishmanial infection can cause a diverse spectrum of diseases, among which VL is the most severe form and which is almost always fatal in more than 95% cases without adequate and timely treatment. Disease occurs in poverty stricken remote areas and affects the poorest people and is associated with malnutrition, population displacement, poor housing conditions and lack of financial resources.

The typical Leishmania (L.) donovani complex is the causative agent of the VL. The species that causes VL is Leishmania donovani in Asia and Eastern Africa and L. infantum in Europe, North Africa and Latin America (Boelaert 2000). The disease is characterized with fever of prolonged duration, weight loss, enlargement of spleen and liver, lymph node enlargement, anemia and low blood cell count. In children other symptoms include diarrhea, cough, abdominal distension, and growth retardation. If disease remains untreated then it progresses to debilitation, bleeding and secondary infections resulting into death. The mode of transmission is anthroponotic and zoonotic. The human-to-human transmission is predominant in east Africa and the Indian sub-continent. The zoonotic transmission is found in the Mediterranean region and the Americas. The zoonotic transmission involved dogs as the main parasitic reservoir (Chappuis 2007).

An estimated 50,000 to 90,000 new cases of VL occur globally every year. of which only 25-45% are reported to WHO. In 2017, more than 95% cases were reported from 10 countries, namely, Bangladesh, Brazil, China, Ethiopia, India, Kenya, Nepal, Somalia, South Sudan and Sudan (WHO Leishmaniasis fact sheet, WHO website, 2019).

In endemic areas, a significant proportion of the healthy individuals are exposed to infection but remain asymptomatic. The ratio between clinical cases and asymptomatic individuals range from 1:5 in Kenay (Schaefer KU, 1995) to 1:8 in Brazil (Evans 1992), 1:5.6 in Ethiopia (Ali A, 1995), 1:8.9 in India and Nepal (Ostyn 2011), and 1:11 and 2.6:1 in Sudan (Zijlstra 1994).

VL treatments are limited, not free from toxic side effects and expensive and because untreated cases result in fatality, it is important that diagnostic tests do not give either give false-negative results which might result in death, nor a false-positive result to avoid people without VL from receiving the toxic treatments (Boelaert 2014).

The gold standard for diagnosis of VL is the microscopic detection of the parasite in specimens. The most sensitive of these techniques is the splenic puncture followed by bone marrow and lymph node aspirates with decreasing order of sensitivity, respectively (Sundar 2002). These are invasive methods and are available only at the referral level and require expertise and equipment. Splenic aspirate has a big disadvantage of risk of a fatal bleeding as a complication of the technique. Therefore, as per the the Kosack et al 2017, ideal diagnostic test for VL endemic settings should comply with the ASSURED criteria of accurate, sensitive, specific, user friendly and robust, equipment-free and is available at the level where they are needed the most. While high sensitivities have been reported in populations of Indian sub-continent (97.0%; 95% CI 90.0 to 99.5), reported sensitivities in East African populations are variable and generally lower (85.3%; 95% CI 74.5 to 93.2).

References:

1. Herwaldt BL. Leishmaniasis. Lancet 1999;354(9185): 1191–9.
2. Boelaert M, Criel B, Leeuwenburg J, Van Damme W, Le Ray D, Van der Stuyft P. Visceral leishmaniasis control: a public health perspective. Transactions of the Royal Society of Tropical Medicine and Hygiene 2000;94(5):465–71.
3. Chappuis F, Sundar S, Hailu A, Ghalib H, Rijal S, Peeling RW, et al. Visceral leishmaniasis: what are the needs for diagnosis, treatment and control?. Nature Reviews Microbiology 2007;5(11):873–82.
4. WHO leishmaniasis fact sheet, WHO, accessed on 25 November 2019, https://www.who.int/news-room/fact-sheets/detail/leishmaniasis
5. Schaefer KU, Kurtzhals JA, Gachihi GS, Muller AS, Kager PA, A prospective sero-epidemiological study of visceral leishmaniasis in Baringo District, Rift Valley Province, Kenya. Trans R Soc Trop Med Hyg. 1995 Sep-Oct; 89(5):471-5.
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7. Ali A, Ashford RW, Visceral leishmaniasis in Ethiopia. IV. Prevalence, incidence and relation of infection to disease in an endemic area., Ann Trop Med Parasitol. 1994 Jun; 88(3):289-93.
8. Ostyn B, Gidwani K, Khanal B, Picado A, Chappuis F, Singh SP, Rijal S, Sundar S, Boelaert M, Incidence of symptomatic and asymptomatic Leishmania donovani infections in high-endemic foci in India and Nepal: a prospective study., PLoS Negl Trop Dis. 2011 Oct; 5(10):e1284.
9. Zijlstra EE, el-Hassan AM, Ismael A, Ghalib HW, Endemic kala-azar in eastern Sudan: a longitudinal study on the incidence of clinical and subclinical infection and post-kala-azar dermal leishmaniasis., Am J Trop Med Hyg. 1994 Dec; 51(6):826-36.
10. Boelaert M, Verdonck K, Menten J, Sunyoto T, van Griensven J, Chappuis F, Rijal S, Rapid tests for the diagnosis of visceral leishmaniasis in patients with suspected disease (Review), Cochrane Database of Systematic Reviews 2014, Issue 6. Art. No.: CD009135.
11. Shyam Sunder and M. Rai, Laboratory Diagnosis of Visceral Leishmaniasis, Clin Diagn Lab Immunol. 2002 Sep; 9(5): 951–958
12. Cara S Kosack, Anne-Laure Page b & Paul R Klatser, A guide to aid the selection of diagnostic tests, Bulletin of the World Health Organization 2017;95:639-645

8. Potential public health impact of the test:

Please explain in which way the proposed test benefits public health. Please detail your response and add references:

Visceral leishmaniasis (VL) is a fatal disease if remains untreated. The signs and symptoms of VL are non-specific. Most patients present with prolonged fever, weight loss, splenic enlargement, loss of appetite, anaemia and other associated illnesses. Other tropical diseases like malaria, tuberculosis, enteric fever share the similar clinical presentation, therefore it is mandatory to follow a clinical-diagnostic algorithm in a clinically suspected case of VL (Chappuis et al 2005). The disease affects some of the poorest populations and is associated with malnutrition, population displacement, poor housing conditions, and a weak immune systems (WHO Leishmaniasis fact sheet, WHO 2019). Therefore, early diagnosis and treatment is the key in controlling the burden of visceral leishmaniasis. Therefore the development of diagnostic tests for improved case management of VL has been rated as one of the most needed among the infectious diseases prevalent in the developing world (Mebey D, 2004)

Anti-leishmanial drugs are expensive and not free from toxicity, it is important to diagnose a case of VL correctly. The gold standard of diagnosis of VL remains the detection of the Leishmania amastigotes parasites in the tissue samples. There are several invasive methods of splenic, bone marrow and lymph node aspirations. However the overall sensitivity varies from 50-90%, splenic (93-99%), bone marrow (53-86%) and lymph nodes (below 50%) (Sundar et al 2012). In addition to variable sensitivities these invasive methods are associated with risks and are painful techniques which require high level of expertise and should be done in referral level hospital. The appropriate tissue extraction and proper staining and examination are other pre-requisites.

Introduction of non-invasive serological tests like the Direct Agglutination Test (DAT) and rK39 based immunochromatographic tests have greatly changed the scenario and have improved the public health impact of early diagnosis of VL patients. DAT was first described in 1975 by Allain and then adapted by El Harith (El Harith, 1986) whereas rK39 was introduced in 1990s (Burns et al 1993).

While rK39 has high sensitivity and specificity in the South-East Asia region Sn (97%; 95% CI 90.0 to 99.5), it has comparatively low and variable sensitivity rates in East African settings (85.3%; 95% CI 74.5 to 93.2) (Boelaert M, 2014; Sundar S, 2002; Mabey D. 2004; Chappuis F 2006; Zilstra EE 2001 and TDR, 2012). Whereas the diagnostic performance of DAT is high in all VL-endemic regions with overall sensitivity and specificity of 95% (93–97%) and 97% (94–99%), respectively, irrespective of the Leishmania species causing VL (L. donovani or Leishmania [L. infantum] (Chappuis F 2006)

rK39 tests are immunochromatographic rapid serological tests, user friendly, cost-effective and can be performed at the community level with test results in maximum 10-20 minutes. These features offer a solution of field diagnosis of VL in remote settings therefore the current WHO recommendation is to use rK39 based rapid diagnostic tests (RDTs) to initiate VL treatment and also use RDTs as the diagnostic tool in the first-line health services in South-East Asia region. In other areas (e.g. East Africa), the RDTs have been used as the first test in diagnosis-treatment algorithms with incorporation of other tests like DAT or invasive procedures of tissue aspirations (Raguenaud 2007; Veeken 2003).

The limitations of DAT is requirement of a cold chain, minimal laboratory conditions and a long incubation period not allowing to give the result in one day.

The WHO Expert Committee Report on the control of the Leishmaniasis recommends to have an additional serological test (e.g. direct agglutination test) or parasitological test in areas where the sensitivity of the rK39 test is below 90% and where results of rK39 is negative in high clinical suspicion of VL in patients with no past history of visceral leishmaniasis. The use of DAT is therefore mentioned in the national guidelines of several VL endemic countries in East Africa.

References:

1. François Chappuis, Yolanda Mueller, Alexandre Nguimfack, John Bosco Rwakimari, Sophie Couffignal, Marleen Boelaert, Philippe Cavailler, Louis Loutan, Patrice Piola, Diagnostic Accuracy of Two rK39 Antigen-Based Dipsticks and the Formol Gel Test for Rapid Diagnosis of Visceral Leishmaniasis in Northeastern Uganda, J Clin Microbiol. 2005 Dec; 43(12): 5973–5977. doi: 10.1128/JCM.43.12.5973-5977.2005
2. WHO leishmaniasis fact sheet, WHO, accessed on 25 November 2019, https://www.who.int/news-room/fact-sheets/detail/leishmaniasis
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Tropical Diseases 2007;1(1):e85
9. Veeken H, Ritmeijer K, Seaman J, Davidson R. Comparison of an rK39 dipstick rapid test with direct agglutination test and splenic aspiration for the diagnosis of kala-azar in Sudan. Tropical Medicine and International Health 2003;8 (2):164–7.

9. Clinical utility of the proposed test/potential impact of the test on patient management and care

Please provide your answer as described in the guidance document:

The invasive methods of diagnosis and associated complications resulted in the development of non-invasive serological tests like direct agglutination test (El Harith, 1986, 1987, 1988). The direct agglutination is a semi-quantitative test and uses microplates in which increasing dilutions of patient's serum or blood is mixed with stained killed promastigotes of Leishmania donovani. The DAT is a freeze-dried suspension of trypsin-treated fixed and stained culture of L. donovani promastigotes. If antibodies against the parasite is present in the sample then agglutination is visible with the naked eyes.

However, the test requires a minimal laboratory set-up, skilled laboratory personnel and a moderate level training to do the test and read the readings (Emily et al, 2012). During infection with VL, circulating antibodies are produced against the surface antigens of the invading parasites. The DAT detects antibodies to L. donovani s.l. in the blood or serum of those infected by means of direct agglutination. In the absence of antibodies to Leishmania the DAT antigen accumulates at the bottom of the plate to form a dark blue spot. If antibodies to Leishmania are present then the antigen forms a pale blue film over the well and this constitutes a positive result (Emily et al, 2012).

The DAT test procedure requires an over night incubation period thus results are not available early. Therefore DAT are recommended at the district hospital level laboratory set up. In spite of these limitations DAT has excellent clinical accuracy resulting in high precision in diagnosing a case of VL. Early and correct diagnosis and timely start of treatment has a major impact on patients outcome and cure of the disease and thus control of the visceral leishmaniasis in the endemic community.

Reference:
1. Harith AE, Kolk AH, Kager PA, Leeuwenburg J, Muigai R, Kiugu S, Kiugu S, Laarman JJ, A simple and economical direct agglutination test for serodiagnosis and sero-epidemiological studies of visceral leishmaniasis, Trans R Soc Trop Med Hyg. 1986; 80(4):583-36
2. Harith AE, Kolk AH, Kager PA, Leeuwenburg J, Faber FJ, Muigai R, Kiugu S, Laarman JJ, Evaluation of a newly developed direct agglutination test (DAT) for serodiagnosis and sero-epidemiological studies of visceral leishmaniasis: comparison with IFAT and ELISA, Trans R Soc Trop Med Hyg. 1987; 81(4):603-6.
3. El Harith, Kolk AH, Leeuwenburg J, Muigai R, Huigen E et al. (1988), Improvement of a direct agglutination test for field studies of visceral leishmaniasis. J Clin Microbiol 26: 1321–1325
4. Adams ER, Jacquet D, Schoone G, Gidwani K, Boelaert M, et al. (2012) Leishmaniasis Direct Agglutination Test: Using Pictorials as Training Materials to
Reduce Inter-Reader Variability and Improve Accuracy. PLoS Negl Trop Dis 6(12): e1946. doi:10.1371/journal.pntd.0001946

10. Systematic reviews of the clinical accuracy of the test

Please describe or comment as requested in guidance document or state if no systematic review of clinical accuracy studies exists:

The direct agglutination test was first described by Allain and Kagan in 1975 followed by adaptation by El Harith et al. A meta-analysis done by Chappuis F, 2006, gives sensitivity and specificity of direct agglutination test in various sub-groups as follows-

Subgroup	No of studies	Sensitivity (95% CI)	No of studies	Specificity (95% CI)
All studies (n=30)	29	94.8 (92.7 to 96.4)	27	97.1 (93.9 to 98.7)
Trial phase:				
I	20	94.3 (91.5 to 96.2)	17	98.1 (94.2 to 99.4)
II	5	97.7 (87.4 to 99.6)	5	97.2 (92.5 to 99.0)
III	4	94.3 (87.9 to 97.4)	5	90.9 (75.9 to 96.9)
Region:				
South Asia	11	97.1 (94.9 to 98.4)	10	95.7 (88.1 to 98.5)
East Africa	11	93.2 (89.1 to 95.8)	10	96.1 (89.2 to 98.6)
Elsewhere	7	92.8 (86.8 to 96.2)	7	99.8 (94.6 to 100)
Leishmania species				
L donovani	23	95.1 (92.7 to 96.7)	21	96.4 (92.5 to 98.4)
Other	6	93.0 (85.1 to 96.9)	6	99.7 (94.6 to 100)
Quality assessment of studies of diagnostic accuracy:				
Score ≤7	19	96.0 (92.5 to 97.9)	17	98.6 (96.7 to 99.4)
Score >7	10	93.7 (90.7 to 95.8)	10	92.6 (83.7 to 96.9)

In summary meta-analysis found DAT to be almost 1% more sensitive and 2% more specific than rK39 strip test.

DAT is an easy to perform, widely applicable technique with high sensitivity (90-100%) and specificity (95-100%) and is routinely used in some regions for the past two decades (Sreenivas et al. 2002;el Harith et al. 2003; el Mutasim et al. 2006;Jacquet et al.2006). The test can be carried out using plasma, serum, or even urine samples, making it suitable for both field and laboratory application (Chappuis et al. 2006; Sundar et al. 2007; Mandal et al. 2008; Bhattarai et al. 2009; Oliveira et al. 2009)

References:

1. Chappuis F, Rijal S, Soto A, Menten J, Boelaert M., A meta-analysis of the diagnostic performance of the direct agglutination test and rK39 dipstick for visceral leishmaniasis, BMJ. 2006 Oct 7;333(7571):723. Epub 2006 Aug 1
2. Sreenivas G, Ansari NA, Singh R, Subba Raju BV, Bhatheja R, Negi NS, Salotra R (2002) Diagnosis of visceral leishmaniasis: comparative potential of amastigote antigen, recombinant antigen and PCR. Br J Biomed Sci 59:218–222
3. el Harith A, el Mutasim M, Mansour D, Fadil Mustafa E, Arvidson H (2003) Use of glycerol as an alternative to freeze-drying for longterm preservation of antigen for the direct agglutination test. Trop Med Int Health 8:1025–1029
4. el Mutasim, Mansour MD, Abass EM, Hassan WM, el Harith A (2006) Evaluation of a glycerol-preserved antigen in the direct agglutination test for diagnosis of visceral leishmaniasis at rural level in eastern Sudan. J Med Microbiol 55:1343–1347
5. Jacquet D, Boelaert M, Seaman J, Rijal S, Sundar S, Menten J, Magnus E (2006) Comparative evaluation of freeze-dried and liquid antigens in the direct agglutination test for serodiagnosis of visceral leishmaniasis (Itma-Dat/Vl). Trop Med Int Health 11:1777–1784
6. Chappuis F, Rijal S, Jha UK, Desjeux P, Karki BM, Koirala S, Loutan L, Boelaert M (2006) Field validity, reproducibility and feasibility of diagnostic tests for visceral leishmaniasis in rural Nepal. Trop Med Int Health 11:31–40
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Comparative evaluation of parasitology and serological tests in the diagnosis of visceral leishmaniasis in India: a phase III diagnostic accuracy study. Trop Med Int Health 12:284–289
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10. Oliveira E, Pedras MJ, de Assis IE, Rabello A (2009) Improvement of direct agglutination test (DAT) for laboratory diagnosis of visceral leishmaniasis in Brazil. Trans R Soc Trop Med Hyg 103:1279–1281

Please attach the reviews you make reference to:

[{ "title":"Meta-analysis","comment":"","size":"108.294","name":"Meta%20analysis_Chappuis_bmj33300723.pdf","filename":"fu_4yqyrk5zviiafpb","ext":"pdf" },{ "title":"Validation of rK39 and DAT_Spain","comment":"","size":"1663.909","name":"validation%20of%20rK39%20and%20DAT.PDF","filename":"fu_ryvs7pp4v7biu5b","ext":"pdf" },{ "title":"Evaluation of freeze-dried DAT","comment":"","size":"67.621","name":"Evaluation%20of%20DAT%20freeze%20dried.pdf","filename":"fu_awpagws3cfq75hs","ext":"pdf" },{ "title":"Multi-centre evaluation of DAT","comment":"","size":"197.278","name":"Multi-centre%20evaluation%20of%20DAT_Boelaert.pdf","filename":"fu_nxxuuaqjgjjpwxv","ext":"pdf" },{ "title":"Systematic review and meta-analysis","comment":"","size":"564.587","name":"Comparative_Study_of_rK39_Leishmania_Antigen_for_S%20%281%29.pdf","filename":"fu_2m2s2esg6c43kak","ext":"pdf" }]

filecount - Please attach the reviews you make reference to:

5

11. Primary studies of clinical accuracy of the test

Please describe or comment as requested in the guidance document or state if no primary studies of clinical accuracy are available:

There have been several validation studies for direct agglutination test for clinical accuracy of the test. A systematic review with meta-analysis of rK39 Leishmania antigen for serodiagnosis of VL comparing with Direct Agglutination Test and Indirect Immunofluorescenee test (IFAT) and ELISA (Zuinara M, 2012) has showed that the sensitivity was 94.23% and specificity 89.97% and the Likelihood ration of a positive test (LR+) 9.39.

In another study in Sudan by Abdullah KA, 2004, The direct agglutination test (DAT) based on freeze-dried (FD) Leishmania donovani antigen was evaluated for the serodiagnosis of kala-azar. The performance of the FD-DAT was compared with standard liquid antigen (LQ) by testing serum and blood samples. The FD-DAT was found to have a sensitivity of 96.8% and a specificity of 96.2.

Please attach the publications you make reference to:

[{ "title":"multi-centre evaluation ","comment":"","size":"197.278","name":"Multi-centre%20evaluation%20of%20DAT_Boelaert.pdf","filename":"fu_hchd3guqrqzarjx","ext":"pdf" },{ "title":"development and application of diagnostic tools for VL","comment":"","size":"67.431","name":"Development_and_application_of_simple_di_Henk.pdf","filename":"fu_nc3gxxj4vi22tdr","ext":"pdf" },{ "title":"Evaluation of DAT and rK39_Henk","comment":"","size":"45.118","name":"Evaluation%20of%20DAT%20and%20rK39_Henk.pdf","filename":"fu_kaqkyz4jamem93q","ext":"pdf" }]

filecount - Please attach the publications you make reference to:

3

12. Systematic reviews of the clinical utility/impact of the test on patient management and care

Please describe any systematic reviews of studies on the impact of the test result in clinical practice on diagnosis, treatment and patient outcomes or state if none are available (please refer to the guidance document)

No systematic reviews are available for the clinical utility or impact of the test on patient management and care. However, several studies are available where it is clearly brought out that the early diagnosis and complete treatment had a positive impact on the control of VL in very high endemic settings.

Please attach the reviews you make reference to:

filecount - Please attach the reviews you make reference to:
0

13. Primary studies of the clinical utility/impact of the test on patient management and care

Please briefly describe any primary studies of the clinical utility/impact of the test on patient management and care, or state if none are available (please refer to the guidance document):
In one study where about 6.2% normal persons in VL endemic areas were found to be reactive to DAT and about 3.6% became seropositive in a year's time (Hasker et al 2013). In another study the same author demonstrated the strong association between serological status and probability of progression to clinical VL in prospective cohort studies in India and Nepal by using DAT titres (Hasker et al 2014). Therefore proving the utility of DAT not only as a diagnostic test but also using it in sero-surveys for field surveillance.

Please include the articles/documents of key primary studies and all publications you make reference to:

filecount - Please include the articles/documents of key primary studies and all publications you make reference to:
0

14. Details of any guideline recommendations concerning use of the test

Briefly describe the specific recommendation (indicate where it can be found in the guideline) and summarise the evidence upon which it is based (indicating where it can be found in the evidence summaries):
1. WHO Technical Report Series 949 2. National guidelines of diagnosis, treatment and prevention of visceral leishmaniasis, Ministry of Health Ethiopia 3. National VL guidelines for Kenya 4. National VL guidelines for Sudan 5. National VL guidelines for South Sudan 6. National VL guidelines for Uganda

Please attach the guidelines that you are refering to:
[{ "title":"Ethiopia VL guidelines","comment":"","size":"3662.351","name":"Guideline_for_diagnosis_treatment_and_prevention_of_leishmaniasis_in_Ethiopia.pdf","filename":"fu_vw8s8v6525i7ieu","ext":"pdf" },{ "title":"Kenya VL guidelines","comment":"","size":"1874.16","name":"Kala_Azar_Kenya_2017.pdf","filename":"fu_s6hru6vx3j2dct2","ext":"pdf" },{ "title":"South Sudan VL guidelines","comment":"","size":"4029.81","name":"Guidelines_for_diagnosis_treatment_and_prevention_of_VL_in_South_Sudan.pdf","filename":"fu_tct9n4tfg9ikhnv","ext":"pdf" },{ "title":"Uganda VL guidelines","comment":"","size":"3117.786","name":"MOH_Uganda_Guidelines_diagnosis_treatment_prevention_VL.pdf","filename":"fu_cqex8kv4twm497r","ext":"pdf" },{ "title":"Sudan VL guidelines","comment":"","size":"386.327","name":"Manual_for_the_diagnosis_and_treatment_Leishmaniasis_Guideline_Sudan_2014%20%281%29.pdf","filename":"fu_5uyfy54txtru4cz","ext":"pdf" },{ "title":"WHO Technical Report Series 949","comment":"","size":"2141.353","name":"WHO_TRS_949_eng.pdf","filename":"fu_qfbkj98i2wpuz49","ext":"pdf" }]

filecount - Please attach the guidelines that you are refering to:
6

15. Examples of commercially available IVD products in the proposed new category

Please download and complete the table in Annex I with commercially available IVD products in the test category, and include the information listed for each one. Please upload the completed file back and all the relevant test Instructions For Use (Package Inserts):
[{ "title":"Annex I","comment":"","size":"16.367","name":"Annex-I-Full-submission.docx","filename":"fu_s74bax6whksnfb8","ext":"docx" },{ "title":"flyer DAT","comment":"","size":"162.955","name":"flyer%20DAT_WHO.pdf","filename":"fu_g8cxbk4z7zk7pdw","ext":"pdf" },{ "title":"Package insert","comment":"","size":"389.193","name":"Package%20insert_PDT_BR_0007_E__4.1.pdf","filename":"fu_7krkcxkve8b6ibw","ext":"pdf" },{ "title":"DAT pictorial","comment":"","size":"710.25","name":"Paper.DAT.pictorials.pdf","filename":"fu_mdrtbeayq6xz4zm","ext":"pdf" }]

filecount - Please download and complete the table in Annex I with commercially available IVD products in the test category, and include the information listed for each one. Please upload the completed file back and all the relevant test Instructions For Use (Package Inserts):
4

16. Training requirements

Considering the tests mentioned in 15 above, what in general are the training requirements?:
One-day training (in person or videoconference)

17. Equipment required

Considering the tests mentioned in 15 above, please describe in general terms what, if any, equipment is required other than that provided with the test:
Minor laboratory equipment are required such as microtiter plates, pipettes, centrifuge machine

18. Energy requirements

Considering the tests mentioned in 15 above, what, if any energy source is required for performance of the tests?:
No external power supply required

Considering the tests mentioned in 15 above, what, if any energy source is required for performance of the tests?: [Other]

19. Landscape reviews

Please list any landscape reviews describing the different test technologies and their use or state if none available:
WHO Manual on Visceral Leishmaniasis Control is attached

Please attach the documents refered to in this question:
[{ "title":"WHO manual on control of VL","comment":"","size":"2717.356","name":"WHO_LEISH_96.40.pdf","filename":"fu_v2euzzn29mcxkb9","ext":"pdf" }]

filecount - Please attach the documents refered to in this question:
1

20. Cost and Cost-effectiveness

Please provide a summary of data on comparative cost and cost-effectiveness or state if not available:
As per Boelaert M, 1999, the availability of DAT has proved convenient for use in field conditions. Since the questions is to choose between an invasive technique (Splenic, bone-marrow or lymph node asipirations) and having a serologic test, it is straightforward case of cost-effective approach to have serological tests (DAT and or rK39). References: 1. M. Boelaert, L. Lynen, P. Desjeux, & P. Van der Stuyft, 1999, Cost-effectiveness of competing diagnostictherapeutic strategies for visceral leishmaniasis, Bulletin of the World Health Organization, 1999, 77 (8)

21. Ethical issues

Please detail any important ethical considerations related to the proposed test category and any consequences of its use:
There are no ethical considerations

22. Equity and human rights issues

Please indicate if it reduces inequities and increases accessibility or if the test may prove inaccessible to some populations:
Availability of serological tests for VL have greatly improved the access to diagnosis and treatment services.

Signature

Through the electronic signature below, I acknowledge that I have provided appropriate information to support this submission. I acknowledge that WHO reserves the right to format and select the information provided as necessary and agree that the information will be publicly disclosed by WHO. [Electronic Signature (type your full name to sign):]
Saurabh Jain

Through the electronic signature below, I acknowledge that I have provided appropriate information to support this submission. I acknowledge that WHO reserves the right to format and select the information provided as necessary and agree that the information will be publicly disclosed by WHO. [Date (yyyy-mm-dd):]
2019-11-26