Laboratory Outreach Communication System (LOCS) Call

Monday, November 13, 2023, at 3:00 P.M. ET

- **Welcome**
  - Jasmine Chaitram, CDC Division of Laboratory Systems
- **SARS-CoV-2 Variants Update**
  - Natalie Thornburg, CDC Coronavirus and Other Respiratory Viruses Division
- **Emergency Use Authorizations for In Vitro Diagnostics**
  - Kim Sapsford-Medintz, U.S. Food and Drug Administration
- ***Brucella* - What's New: Changes and Challenges**
  - Kurt Jerke, U.S. Army
- **An Upgrade for the LOCS Website: New Search and Filter Functionality**
  - James Bratton, CDC Division of Laboratory Systems

About DLS

Vision

Exemplary laboratory science and practice advance clinical care, public health, and health equity.

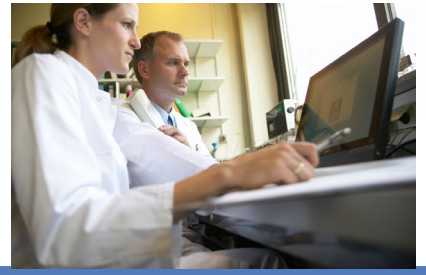
Four Goal Areas

Quality Laboratory Science

- Improve the quality and value of laboratory medicine for better health outcomes and public health surveillance

Highly Competent Laboratory Workforce

- Strengthen the laboratory workforce to support clinical and public health laboratory practice



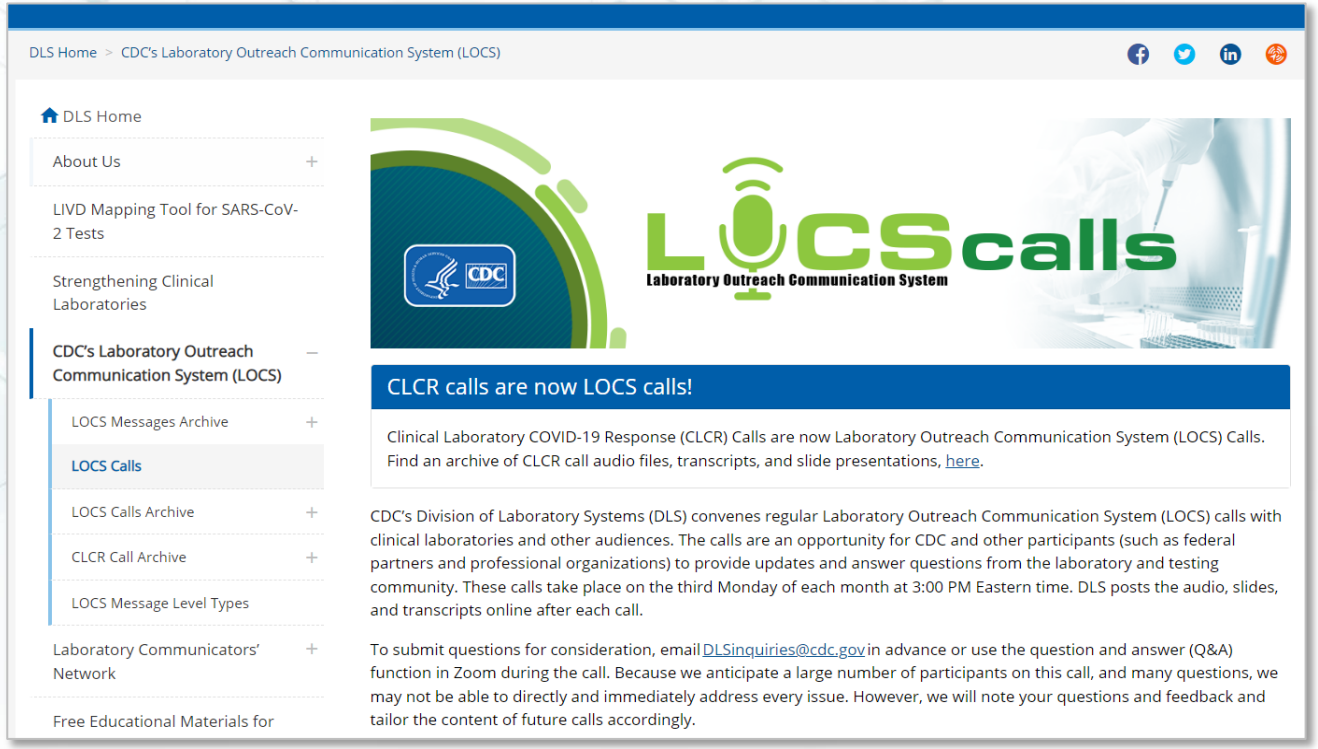
Safe and Prepared Laboratories

- Enhance the safety and response capabilities of clinical and public health laboratories

Accessible and Usable Laboratory Data

- Increase access and use of laboratory data to support response, surveillance, and patient care

LOCS Calls



On this page, you can find:

- LOCS Call information
- Transcripts
- Slides
- Audio Recordings

https://www.cdc.gov/locs/calls

We Want to Hear From You!

Training and Workforce Development

Questions about education and training?

Contact LabTrainingNeeds@cdc.gov

OneLab **REACH™**

Fundamentals of Communicating the Hazards of Laboratory Chemicals

This basic level course is designed for public health and clinical laboratory staff, safety professionals, and others who work in laboratories where hazardous chemicals are routinely used and stored. It introduces OSHA Standards and their role in providing information to laboratory staff.

REGISTER NOW

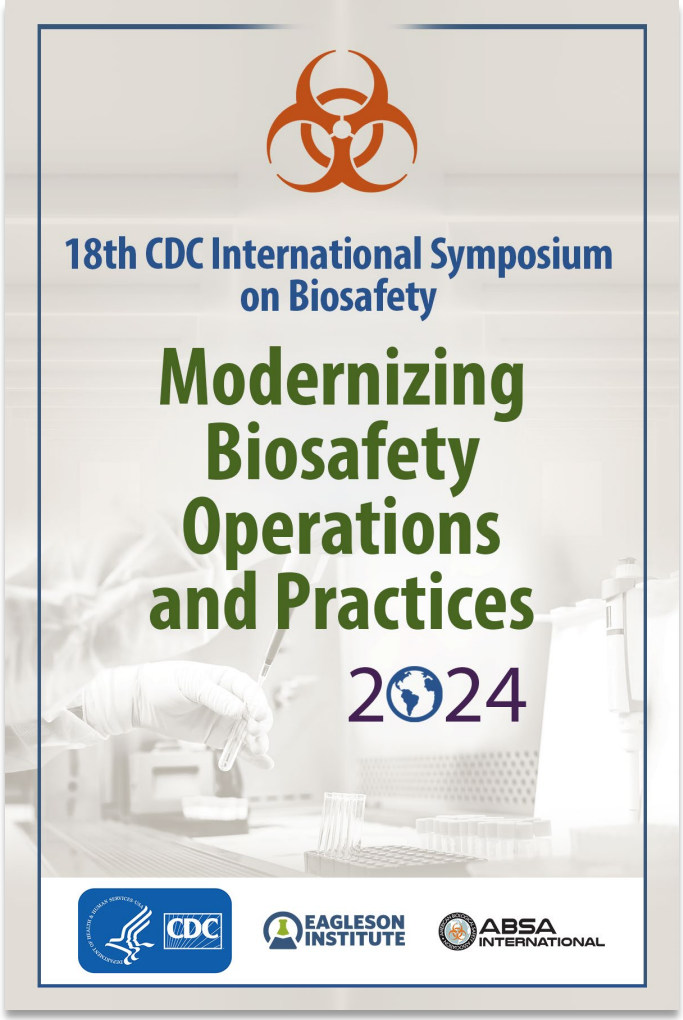
P.A.C.E.® credit

This course is 1 contact hour(s)

CDC International Symposium on Biosafety

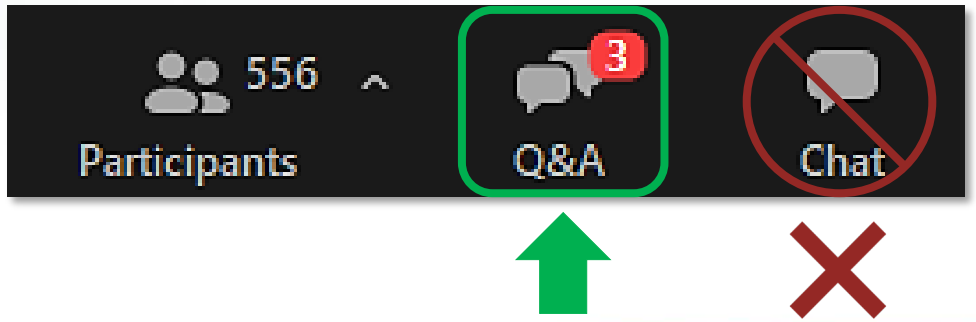
- March 10-14, 2024
- Crowne Plaza Ravinia, Atlanta, GA
- The symposium will provide sessions about modernizing biosafety operations and practices, focused on the areas of Clinical Care, Public Health, Research, and Animal Care

https://www.eagleson.org/conferences/cdc-international-biosafety-symposium/



How to Ask a Question

- **Using the Zoom Webinar System**
  - Click the **Q&A button** in the Zoom webinar system
  - Type your question in the **Q&A box** and submit it
  - Please do not submit a question using the chat button



- For media questions, please contact CDC Media Relations at media@cdc.gov
- If you are a patient, please direct any questions to your healthcare provider

Slide decks may contain presentation material from panelists who are not affiliated with CDC. Presentation content from external panelists may not necessarily reflect CDC's official position on the topic(s) covered.

SARS-CoV-2 Variants Update

Natalie Thornburg, PhD
CDC Coronavirus and Other Respiratory Viruses Division

Emergency Use Authorizations for IVDs

Kim Sapsford-Medintz
FDA/CDRH/OHT7-OIR/DMD
Kim.Sapsford@fda.hhs.gov

Overview

- Why are EUAs Needed?
- EUA Authority and Criteria
- EUA Versus Traditional Marketing Submissions
- EUA Documentation
- Post EUA

Why are Legal/Regulatory Mechanisms for Emergency Use of Medical Products Needed?

Without legal mechanisms, certain preparedness and response activities could otherwise violate provisions of the Federal Food, Drug, and Cosmetic (FD&C) Act:

- Products needed for a response might not be approved, licensed, or cleared by FDA
- Products needed for a response might be approved by FDA, but not for the emergency use (e.g., for a new indication)
- Ensures any available HHS Public Readiness and Emergency Preparedness (PREP) Act protections apply
- Facilitates Import or Export and distribution of the product.
- Facilitates pre-positioning of MCM products for emergency use upon authorization

EUA Authority (FD&C Act § 564)

Chemical C

Biological B

Radiological R

Nuclear N

67

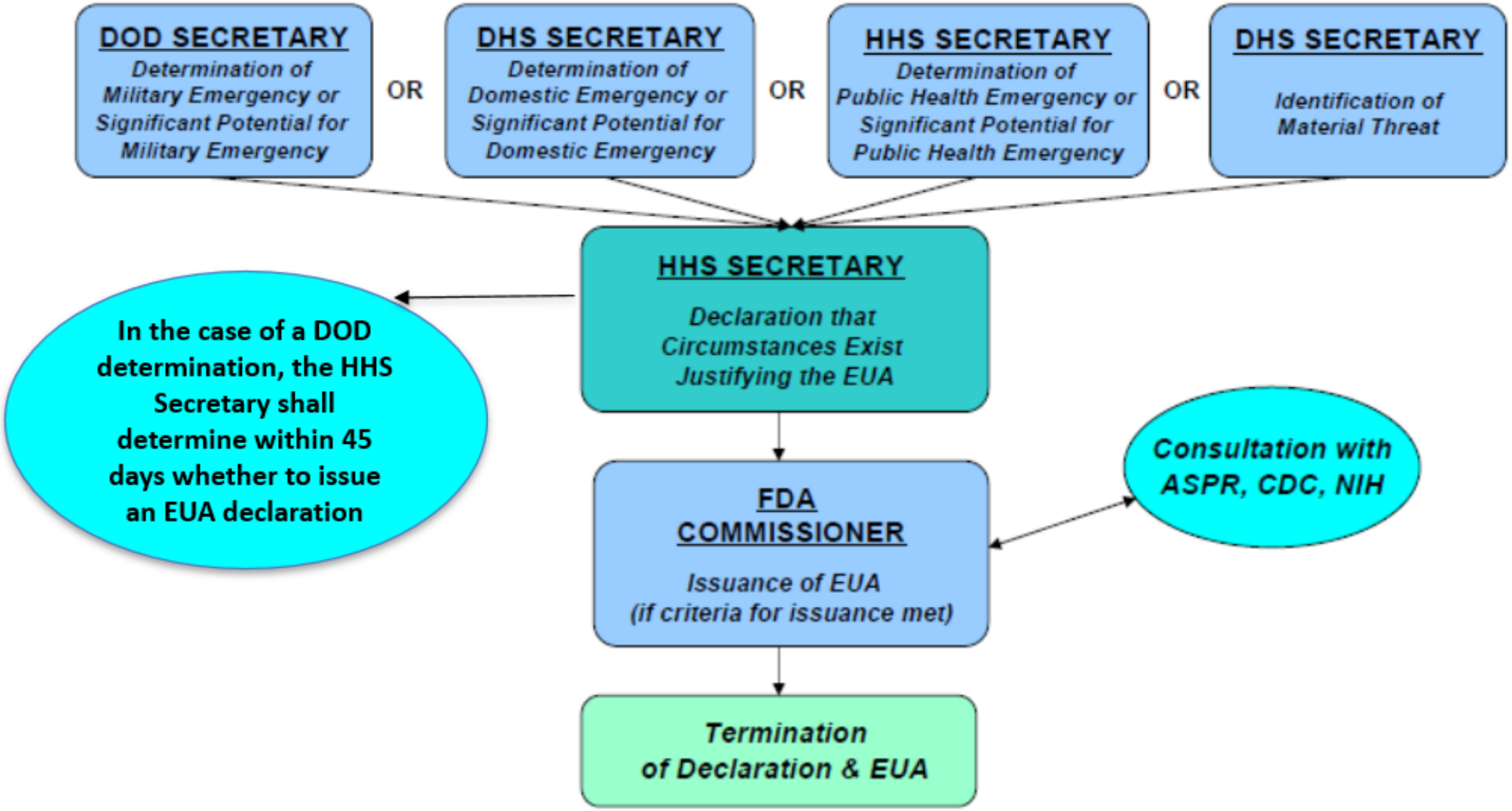
With an EUA, FDA can authorize:

- Use of unapproved Medical Counter Measures (MCMs) (despite lacking the amount of data that would be necessary for approval)
- Unapproved use of approved MCMs (e.g., for a new indication)

to **diagnose**, treat, or prevent serious or life-threatening diseases or conditions caused by CBRN threat agents **when certain criteria and pre-requisites are met**

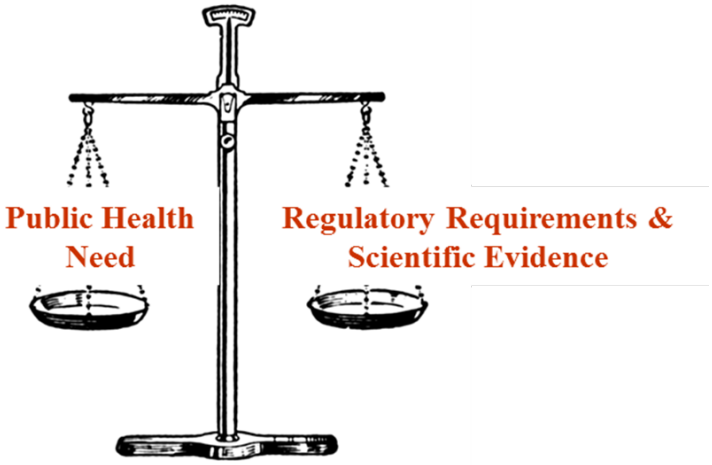
In addition, DoD may issue a determination based on '*an agent or agents that may cause, or are otherwise associated with, an imminently life-threatening and specific risk to United States military forces*'

EUA Pre-Requisites: Determination and Declaration



EUA Criteria

- Main Criteria:
  - ➢ Serious or life-threatening disease or condition caused by an agent
  - ➢ Based on **totality of scientific evidence**, reasonable belief:
    - Product **may be** effective
    - Known/potential benefits outweigh known/potential risks (Each product is assessed independently, based on circumstances at time of request)
  - ➢ No adequate, approved, available alternative to the product



Nucleic Acid Amplification Test (NAAT)	De novo or 510(k)	Emergency Use Authorization (EUA)
Limit of Detection (LoD)	Yes	?
Inclusivity	Yes Some *in silico*	?
Exclusivity	Yes Some *in silico*	?
Interference	Yes	?
Precision/Repro.	Precision: Yes – Single-site/within site Repro.: Yes – Multi-site	?
Fresh vs. Frozen	Fresh specimens preferred	?
Specimen Stability	Yes	?
Reagent Stability	Yes	?
Clinical Evaluation	Yes – natural clinical specimens	?

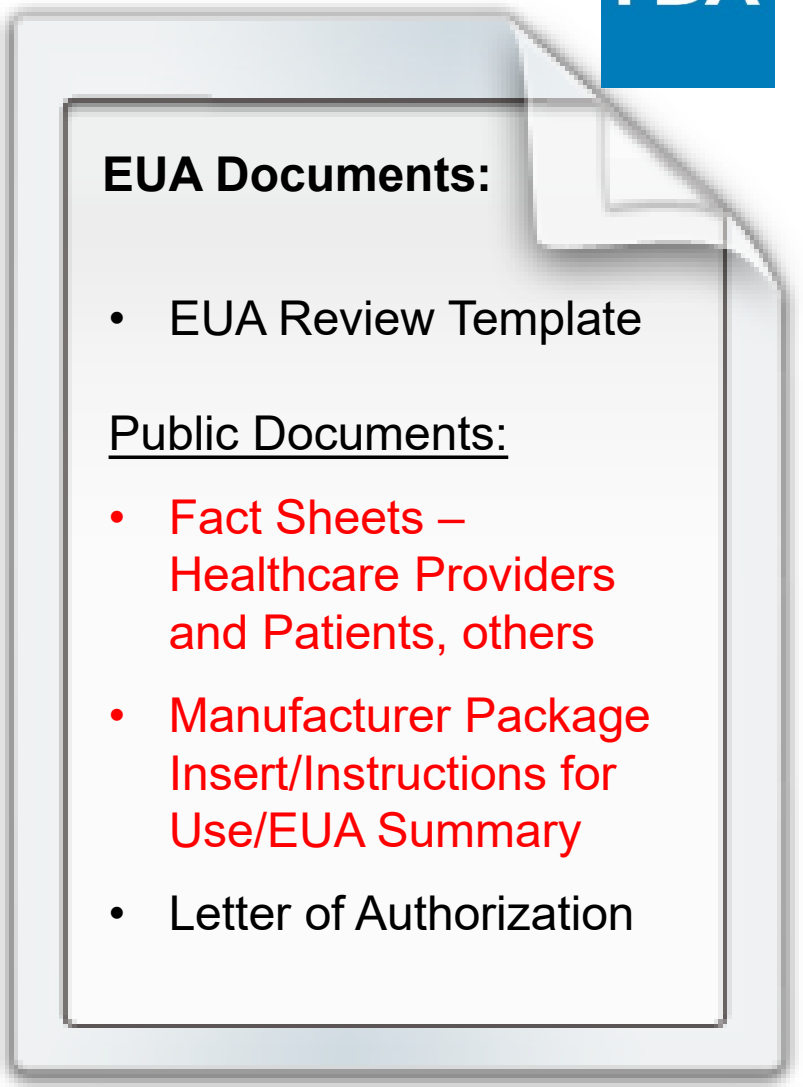
Scientific Evidence

Nucleic Acid Amplification Test (NAAT)	De novo or 510(k)	Emergency Use Authorization (EUA)
Limit of Detection (LoD)	Yes	Yes
Inclusivity	Yes Wet testing, plus some *in silico*	Yes - Technology dependent - in silico acceptable if applicable
Exclusivity	Yes Wet testing, plus some *in silico*	Limited - Technology dependent - in silico acceptable if applicable
Interference (Substances and microbiol.)	Yes	Technology specific – not always required if technology includes an extraction step for example
Precision/Repro.	Precision: Yes – Single-site/within site Repro.: Yes – Multi-site	No
Fresh vs. Frozen	Fresh specimens preferred	Fresh specimens preferred
Specimen Stability	Yes	Depends – needed if claims are outside of CDC recommendations
Reagent Stability	Yes	No – However, study design required
Clinical Evaluation	Yes – natural clinical specimens – prospective multi-site clinical study	Limited – natural clinical specimens if available at the time

EUA Documents

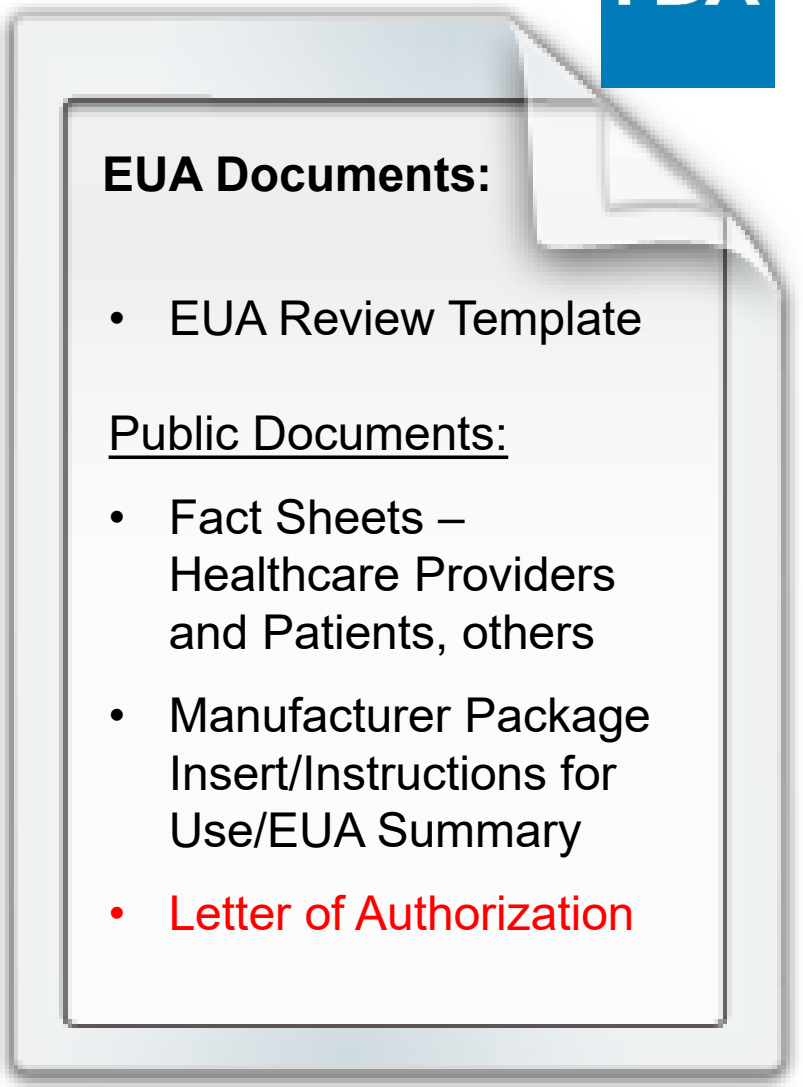
- **EUA Fact Sheets:**
  - The EUA Fact Sheets pertain to the emergency use of the product and outline the associated benefits and risks associated with its use
  - FDA typically develop Healthcare Provider/Professional or other authorized dispenser and Patient/Recipient Fact Sheet templates specific to the PHE and will share these with test/kit developers during the review of their EUA submission

- **Manufacturer Package Insert/Instructions for Use/EUA Summary/Standard Operating Procedures**:
  - Described how to perform the test and/or use the EUA product
  - Summarizes the analytical and clinical performance FDA used to assess the benefit risk of the EUA product in its intended use



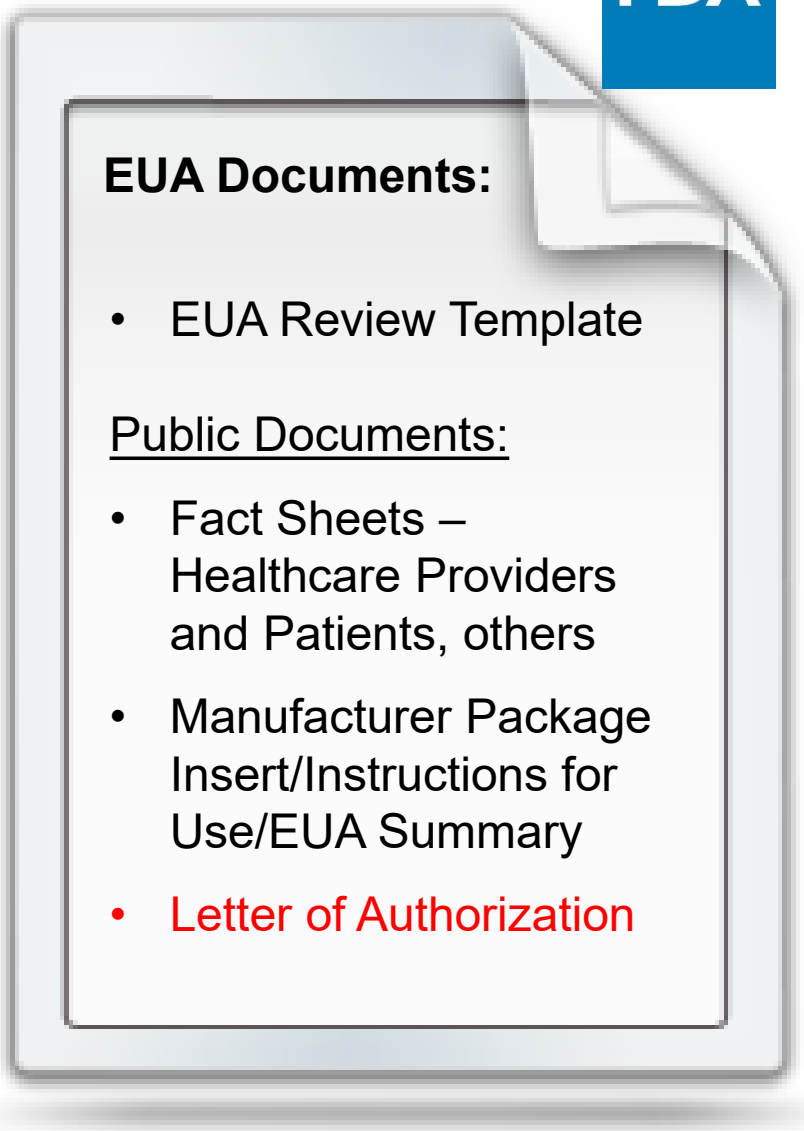
EUA Documents

- **Letter of Authorization**:
  - The Letter of Authorization authorizes the emergency use of the test and allows the test to be distributed in the U.S.
  - The letter includes the criteria for issuance of authorization and the scope of authorization.
  - The letter includes the Conditions of Authorization that are required to be met by the applicable parties.
    - Manufacturer
    - Distributors – includes 3rd party
    - Laboratories
    - Others



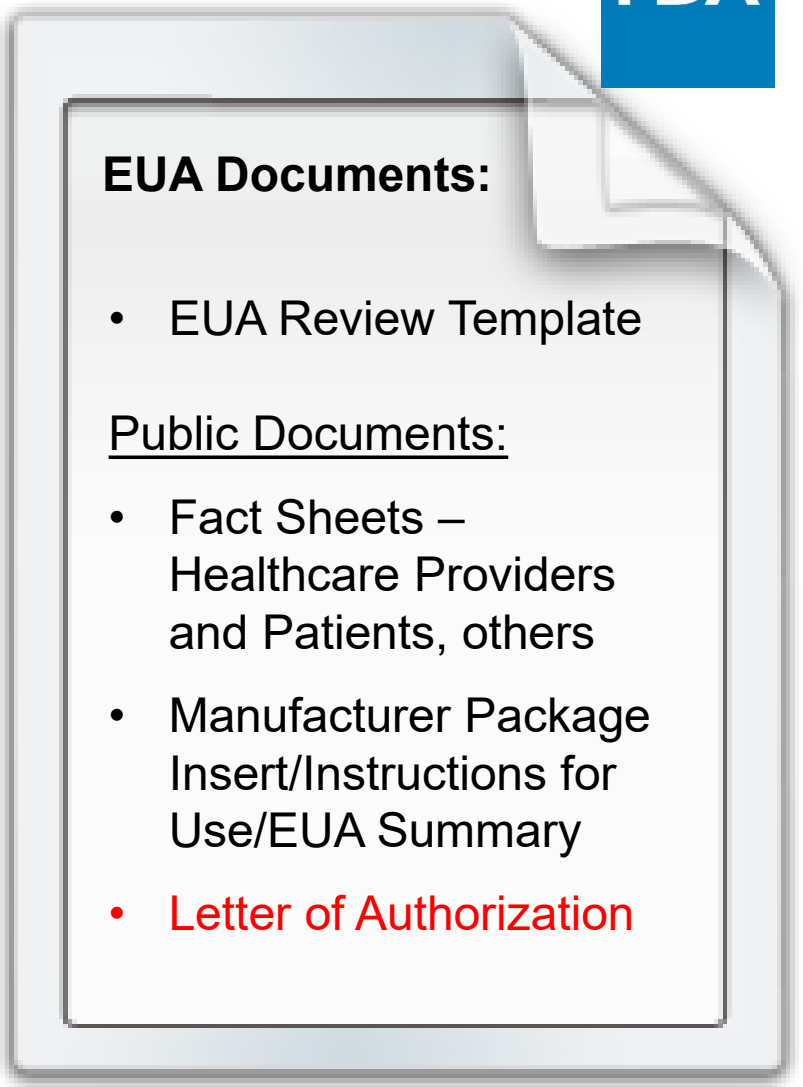
EUA Documents

- **Letter of Authorization**:
  - The letter can also include (if applicable) the waiver of certain requirements otherwise required by applicable federal law.
    - Current good manufacturing practice requirements, including the quality system requirements under 21 CFR Part 820 with respect to the design, manufacture, packaging, labeling, storage, and distribution of your product, but excluding Subpart H (Acceptance Activities, 21 CFR 820.80 and 21 CFR 820.86), Subpart I (Nonconforming Product, 21 CFR 820.90), and Subpart O (Statistical Techniques, 21 CFR 820.250).



EUA Documents

- **Letter of Authorization - Conditions of Authorization:**
  - Distribution of the EUA product, manufacturing and labeling
  - Registration and listing requirements
  - Outlines how changes to the EUA product can be requested and made
  - Reporting of test results and adverse events
  - Outlines certain content required for descriptive printed matter, advertising, and promotional materials
  - Outlines required post-authorization studies that the test-developer must complete or agree to as a condition of authorization
    - Real-time reagent stability studies
    - Re-evaluation of analytical or clinical studies
    - Submitting the product for an independent evaluation
    - Testing of a recommended reference material
    - Continued evaluation of microorganism mutations
  - It is important for all parties involved in the manufacture, distribution, and use of the authorized product to be familiar with the content of the Letter of Authorization and associated Conditions of Authorization.



Information Publicly Available on FDA Website

https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations-medical-devices

Information Publicly Available on FDA Website

s/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas-molecular-diagnostic-tests-sars-cov-2

for Multi-analyte Respiratory Panel Tests are accepted the CPT Pathogen code.

Search:

Show 25 entries

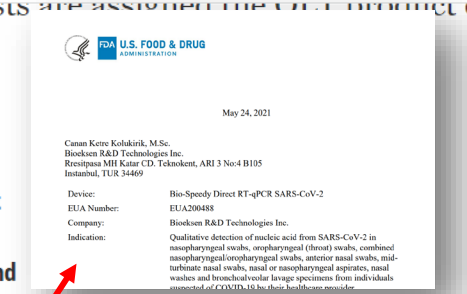
Date EUA Issued or Last Updated	Entity	Diagnostic (Most Recent Letter of Authorization) and Date EUA Original Issue	Attributes[3]	Authorized Setting(s)[1]	Authorization Documents[2]
03/31/2023	Bioeksen R&D Technologies Inc.	Bio-Speedy Direct RT-qPCR SARS-CoV-2 09/02/2020	Real-time RT-PCR, Single Target	H	HCP, Patients, IFU
03/31/2023	Thermo Fisher Scientific Inc.	TaqPath COVID-19 RNase P Combo Kit 2.0 07/08/2021	Real-time RT-PCR, Screening, Home Collection, Multiple Targets	H	HCP, Patients, IFU
03/30/2023	SD Biosensor, Inc.	STANDARD M nCoV Real-Time Detection Kit 04/23/2020	Real-time RT-PCR, Multiple Targets	H	HCP, Patients, IFU

Other Documents

- Letter Granting EUA Revision(s) (December 9, 2020)
- Viral Mutation Revision Letter - September 23, 2021

Other Brand Name(s)

- BioXsen SARS-CoV-2 RT PCR

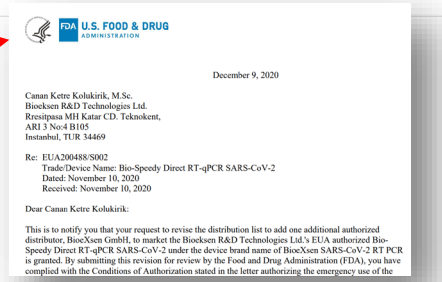


FDA U.S. FOOD & DRUG ADMINISTRATION

May 24, 2021

Canan Ketre Kolukirik, M.Sc.
Bioeksen R&D Technologies Inc.
Resitpasa MH Katar CD. Teknokent, ARI 3 No:4 B105
Instanbul, TUR 34469

Device:	Bio-Speedy Direct RT-qPCR SARS-CoV-2
EUA Number:	EUA200488
Company:	Bioeksen R&D Technologies Inc.
Indication:	Qualitative detection of nucleic acid from SARS-CoV-2 in nasopharyngeal swabs, oropharyngeal (throat) swabs, combined nasopharyngeal/oropharyngeal swabs, anterior nasal swabs, mid-turbinate nasal swabs, nasal or nasopharyngeal aspirates, nasal washes and bronchoalveolar lavage specimens from individuals suspected of COVID-19 by their healthcare provider



FDA U.S. FOOD & DRUG ADMINISTRATION

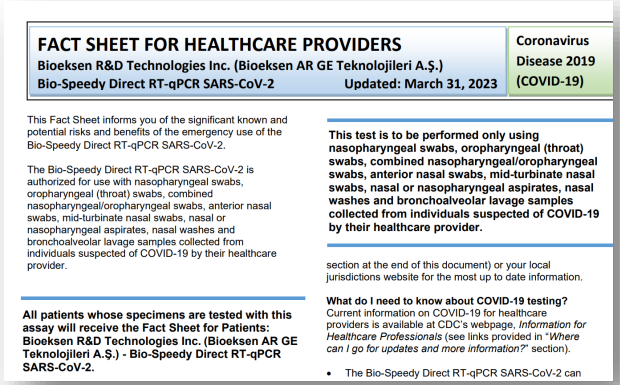
December 9, 2020

Canan Ketre Kolukirik, M.Sc.
Bioeksen R&D Technologies Ltd.
Resitpasa MH Katar CD. Teknokent,
ARI 3 No:4 B105
Instanbul, TUR 34469

Re: EUA200488/S002
Trade/Device Name: Bio-Speedy Direct RT-qPCR SARS-CoV-2
Dated: November 10, 2020
Received: November 10, 2020

Dear Canan Ketre Kolukirik:

This is to notify you that your request to revise the distribution list to add one additional authorized distributor, BioeXsen GmbH, to market the Bioeksen R&D Technologies Ltd.'s EUA authorized Bio-Speedy Direct RT-qPCR SARS-CoV-2 under the device brand name of BioeXsen SARS-CoV-2 RT PCR is granted. By submitting this revision for review by the Food and Drug Administration (FDA), you have complied with the Conditions of Authorization stated in the letter authorizing the emergency use of the



FACT SHEET FOR HEALTHCARE PROVIDERS
Bioeksen R&D Technologies Inc. (Bioeksen AR GE Teknolojileri A.Ş.)
Bio-Speedy Direct RT-qPCR SARS-CoV-2 **Updated: March 31, 2023**
Coronavirus Disease 2019 (COVID-19)

This Fact Sheet informs you of the significant known and potential risks and benefits of the emergency use of the Bio-Speedy Direct RT-qPCR SARS-CoV-2.

The Bio-Speedy Direct RT-qPCR SARS-CoV-2 is authorized for use with nasopharyngeal swabs, oropharyngeal (throat) swabs, combined nasopharyngeal/oropharyngeal swabs, anterior nasal swabs, mid-turbinate nasal swabs, nasal or nasopharyngeal aspirates, nasal washes and bronchoalveolar lavage samples collected from individuals suspected of COVID-19 by their healthcare provider.

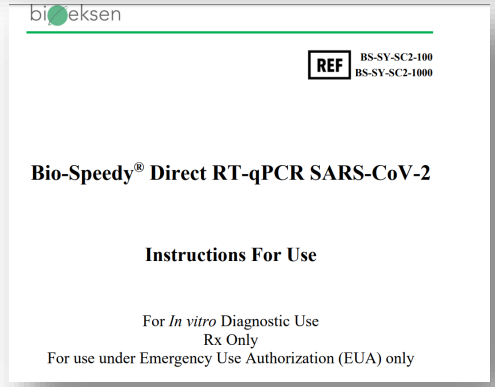
All patients whose specimens are tested with this assay will receive the Fact Sheet for Patients: Bioeksen R&D Technologies Inc. (Bioeksen AR GE Teknolojileri A.Ş.) - Bio-Speedy Direct RT-qPCR SARS-CoV-2.

This test is to be performed only using nasopharyngeal swabs, oropharyngeal (throat) swabs, combined nasopharyngeal/oropharyngeal swabs, anterior nasal swabs, mid-turbinate nasal swabs, nasal or nasopharyngeal aspirates, nasal washes and bronchoalveolar lavage samples collected from individuals suspected of COVID-19 by their healthcare provider.

section at the end of this document) or your local jurisdictions website for the most up to date information.

What do I need to know about COVID-19 testing?
Current information on COVID-19 for healthcare providers is available at CDC's webpage, *Information for Healthcare Professionals* (see links provided in "*Where can I go for updates and more information?*" section).

- The Bio-Speedy Direct RT-qPCR SARS-CoV-2 can



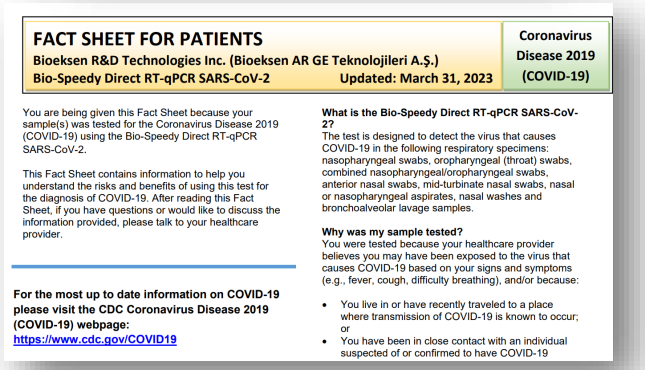
bioeksen

REF BS-SY-SC2-100 BS-SY-SC2-1000

Bio-Speedy® Direct RT-qPCR SARS-CoV-2

Instructions For Use

For *In vitro* Diagnostic Use
Rx Only
For use under Emergency Use Authorization (EUA) only



FACT SHEET FOR PATIENTS
Bioeksen R&D Technologies Inc. (Bioeksen AR GE Teknolojileri A.Ş.)
Bio-Speedy Direct RT-qPCR SARS-CoV-2 **Updated: March 31, 2023**
Coronavirus Disease 2019 (COVID-19)

You are being given this Fact Sheet because your sample(s) was tested for the Coronavirus Disease 2019 (COVID-19) using the Bio-Speedy Direct RT-qPCR SARS-CoV-2.

This Fact Sheet contains information to help you understand the risks and benefits of using this test for the diagnosis of COVID-19. After reading this Fact Sheet, if you have questions or would like to discuss the information provided, please talk to your healthcare provider.

For the most up to date information on COVID-19 please visit the CDC Coronavirus Disease 2019 (COVID-19) webpage:
https://www.cdc.gov/COVID19

What is the Bio-Speedy Direct RT-qPCR SARS-CoV-2?
The test is designed to detect the virus that causes COVID-19 in the following respiratory specimens: nasopharyngeal swabs, oropharyngeal (throat) swabs, combined nasopharyngeal/oropharyngeal swabs, anterior nasal swabs, mid-turbinate nasal swabs, nasal or nasopharyngeal aspirates, nasal washes and bronchoalveolar lavage samples.

Why was my sample tested?
You were tested because your healthcare provider believes you may have been exposed to the virus that causes COVID-19 based on your signs and symptoms (e.g., fever, cough, difficulty breathing), and/or because:

- You live in or have recently traveled to a place where transmission of COVID-19 is known to occur; or
- You have been in close contact with an individual suspected of or confirmed to have COVID-19

Post EUA

FDA's role once an entity is issued an EUA:

- Follow up quickly with manufacturers if potential issues with performance are observed e.g., false positive or false negative
- Monitor supply and device usage as applicable
- Effectively authorize modifications to EUA through Supplements (e.g., new specimen types, instruments) – either trigger a re-issue of the EUA or are granted at the Division level.
- Follow up on reports of misuse of test and/or fraudulent claims
- EUA revocations – posted on the FDA Historical webpage
- 564 Declaration Terminations

Thank You!

Resources:

- CDRH – EUA Page: https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations-medical-devices
- FDA – EUA Page: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization
- CDRH - COVID IVD EUA Page: https://www.fda.gov/medical-devices/covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas
- CDRH - Mpox IVD EUA Page: https://www.fda.gov/medical-devices/emergency-use-authorizations-medical-devices/monkeypox-mpox-emergency-use-authorizations-medical-devices
- CDRH - Historical EUA Webpage: https://www.fda.gov/medical-devices/emergency-use-authorizations-medical-devices/historical-information-about-device-emergency-use-authorizations
- CDRH Device Databases: https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/medical-device-databases

COVID-19 Product Codes	De Novo and 510k Products
QOF	Multi-Target Respiratory Specimen Nucleic Acid Test Including Sars-Cov-2 And Other Microbial Agents
QWR	Simple Point-Of-Care Device To Detect Sar-Cov-2 Nucleic Acid Targets From Clinical Specimens In Near-Patient Settings
QQX	Respiratory Specimen Nucleic Acid Sars-Cov-2 Test
QVF	Simple Point-Of-Care Device To Directly Detect Sars-Cov-2 Viral Targets From Clinical Specimens In Near-Patient Settings
QVP	Sars-Cov-2 Serology Test
QWB	Over-The-Counter Molecular Test To Detect Sars-Cov-2 From Clinical Specimens

Brucella

What's New: Changes and Challenges

Laboratory Outreach Communication System
November 13th, 2023

Kurt Jerke, Ph.D., D(ABMM)

AMERICAN SOCIETY FOR MICROBIOLOGY

Disclosure

- **The views and opinions expressed or implied in this presentation are solely those of the authors and should not be construed as policy or carrying the official sanction of the United States Army, the Department of Defense, United States Military Academy, or other agencies or departments of the US government.**

Outline

- Select agent species
- Reclassification of *Ochrobactrum* to *Brucella*
- Updates to the ASM-APHL Sentinel Level Guidelines
- Gram stain and misidentification
- Questions

Select Agent *Brucella S*pecies

- Gram-negative coccobacilli (0.4 x 0.8 µM)
- Causative agent of brucellosis
- Zoonotic bacteria
  - *B. melitenensis** – Sheep and Goats
  - *B. suis** – Pigs, hares, wild rodents
  - *B. abortus** - Cattle
  - *B. canis* - Dogs

*** Classified as a biological select agent**

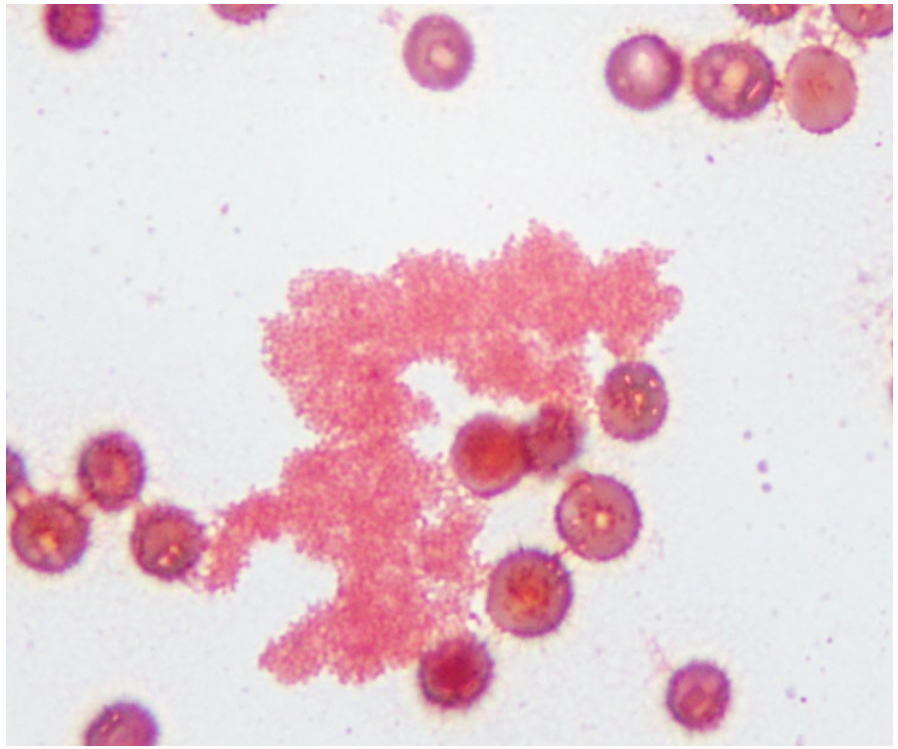


Photo courtesy of Erin McElvania

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Select Agent *Brucella S*pecies

- Brucellosis
  - Acute disease -fever, headache, myalgia, arthralgia
  - Chronic disease – recurrent fever, fatigue, joint pain
- Low infectious dose (10 to 100 microorganisms)
- Routes of exposure
  - Laboratory
  - Food
  - Animal (occupational and recreation)

Taxonomic Changes

- *Ochrobactrum* genus designated in 1988
  - Non enteric, aerobic Gram negative rods, **motile**, acid from several carbohydrates
  - Environmental organisms – Soil, water, plants, animals
  - Opportunistic pathogen, generally low virulence
- In 2020 Hordt et. al proposed reclassifying *Ochrobactrum* to the genus *Brucella* based on genome analysis
- Both the original *Ochrobactrum* and *Brucella* species names are currently considered valid
- *Brucella* (*Ochrobactrum*) species do not cause brucellosis and are **not** classified as biological select agents

Considerations and Implications

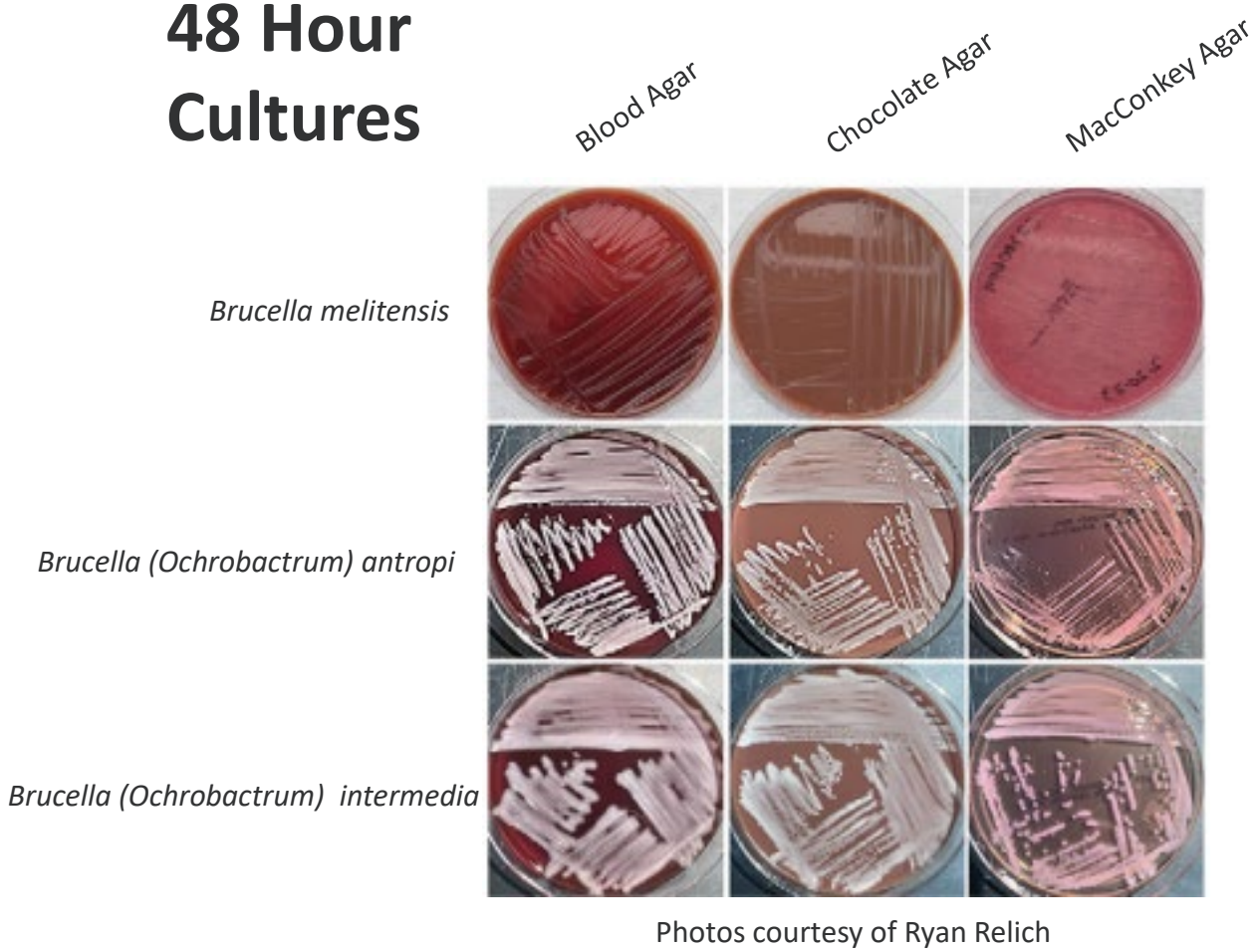
- Reporting
  - Both nomenclature are still considered valid
  - CAP requires taxonomic updates under certain conditions (MIC.11375)
    - Labs should ensure the correct antimicrobial susceptibility breakpoints are applied to each organism
  - Important to communicate with clinical staff
    - *Brucella (Ochrobactrum)* does not cause brucellosis
    - Is not a select agent (must rule out select agent *Brucella* species)

Considerations and Implications

- Antimicrobial Susceptibility Testing
  - Refer possible select agent species to a LRN reference lab
  - *Brucella* (*Ochrobactrum*): if following CLSI standards, apply "Other Non-Enterobacterales" methods and interpretations
- Biosafety Requirements
  - Select agent *Brucella* species require BSL-3 or BSL-2 w/ BSL-3 precautions
  - *Brucella* (*Ochrobactrum*) can be handled safely using standard BSL-2 precautions

Updates to the ASM-APHL Sentinel Guidelines

- Common characteristics that differentiate *Brucella* (*Ochrobactrum*) from select agent *Brucella* species
  - Rapid growth on MacConkey
  - Mucoid colony morphology
  - Positive motility (tube based)
- Revised guidelines under final review by ASM and APHL
- Thank you to both organizations for their work



Photos courtesy of Ryan Relich

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Gram Stain Misidentification

- Recent reports of *Brucella* staining Gram positive
  - One Case reported from WA, *B. melitensis* (2019)
  - Two cases from RI, *B. melitensis*, *B. abortus* (2022)
  - Three cases from NY, *B. melitensis* (2), *B. abortus* (2020)
  - One case from Saudi Arabia *Brucella* species (2017)
- All specimens were blood culture
  - Time to detection typically 24 to 96 hrs
  - Gram stain from bottle reported as Gram positive rods or cocci
  - Subcultures were Gram variable or Gram negative

Gram Stain Reaction and Morphology May be Atypical

Typical

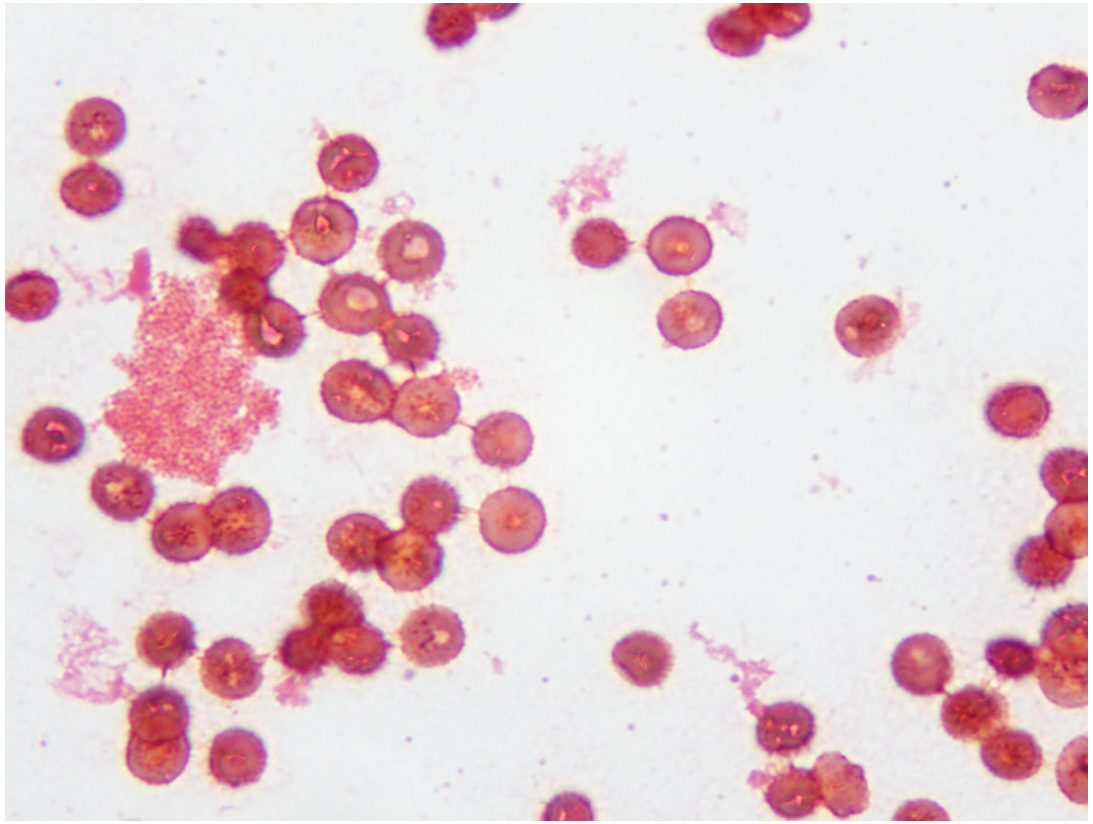

Photo courtesy of Erin McElvania

Typical Morphology:

- Small coccobacilli
- Gram negative
- Often aggregate

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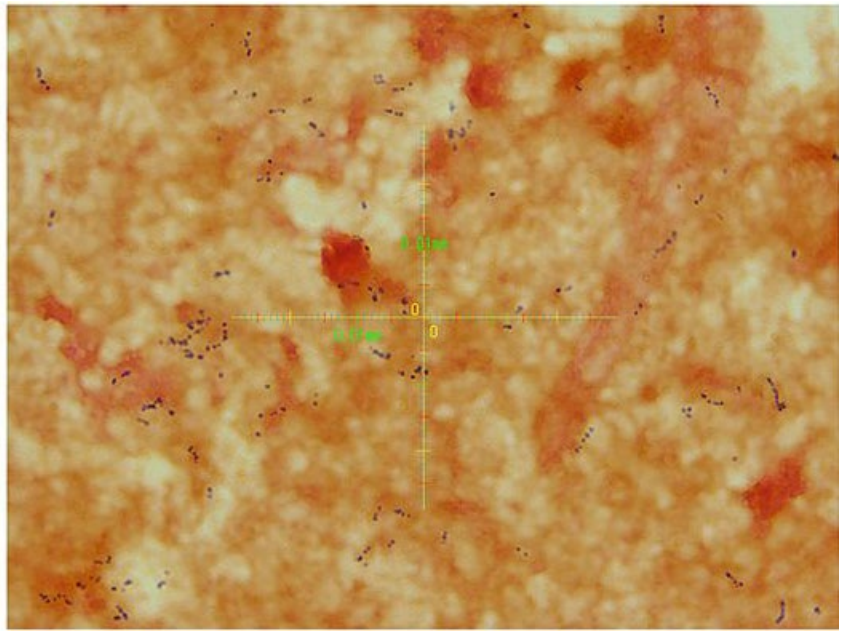
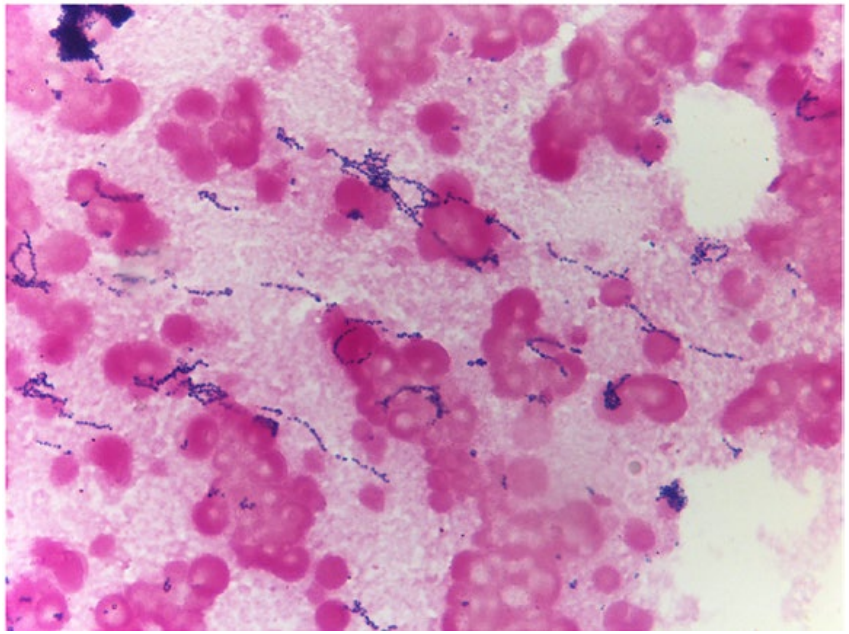
Gram Stain Reaction and Morphology May be Atypical

Atypical



Atypical



Atypical Morphologies:

- Coccobacilli to rods
- Gram variable or gram positive
- Singles, pairs, or chains
- Aggregates may not be seen

Photos from Ackelberg et al. doi.org/10.1128/JCM.01096-19.

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Gram Stain Misidentification

- Highlights importance of communication between laboratory and clinicians
- Education and training for laboratory staff
- Reconsider laboratory processes
  - Manipulation of all slow growing organisms in a biological safety cabinet

Thank You!

Questions? Contact Us.

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An Upgrade for the LOCS Website: New Search and Filter Functionality

James Bratton, MA
CDC Division of Laboratory Systems

LOCS Website Upgrade

- Earlier this autumn, the Division of Laboratory Systems added search and filter functions to the website
- These new functions make it easier to search through the more than 300 LOCS messages archived on our website
- Messages date back to the website's inception, in 2017
- To contact us about the website, please email LOCS@cdc.gov with the subject line "LOCS website feedback"
- https://www.cdc.gov/locs/index.html

Next Scheduled Call

Monday, December 18
3 PM - 4 PM EDT

https://www.cdc.gov/locs/calls

CDC Social Media

https://www.facebook.com/CDC

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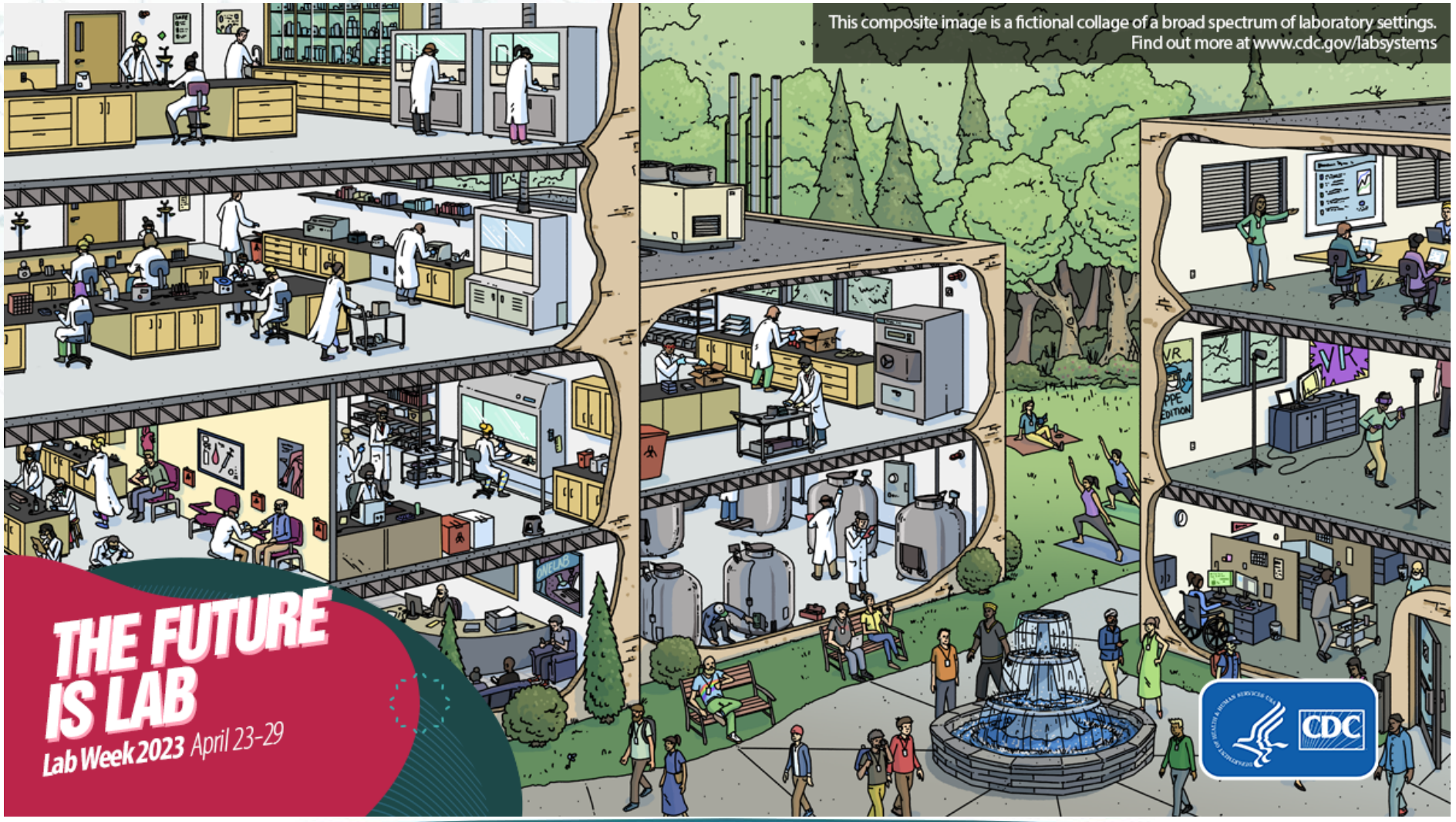
https://www.instagram.com/cdcgov

https://www.linkedin.com/company/cdc

Thank You For Your Time!



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov