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UTILITY PATENT APPLICATION TRANSMITTAL (Only for new nonprovisional applications under 37 CFR 1.53(b))		Attorney Docket No. OSHH-001/C05US	
		First Named Inventor Youssef BIADILLAH	
		Title BIOLOGICAL COLLECTION SYSTEM	
		Priority Mail Express® Label No.	

APPLICATION ELEMENTS See MPEP chapter 600 concerning utility patent application contents.	ADDRESS TO: Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450
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1. ☐ Fee Transmittal Form (PTO/SB/17 or equivalent) 2. ☐ Applicant asserts small entity status. See 37 CFR 1.27 3. ☐ Applicant certifies micro entity status. See 37 CFR 1.29. Applicant must attach form PTO/SB/15A or B or equivalent. 4. ☒ Specification [Total Pages <u>36</u>] Both the claims and abstract must start on a new page. (See MPEP § 608.01(a) for information on the preferred arrangement) 5. ☒ Drawing(s) (35 U.S.C. 113) [Total Sheets <u>9</u>] 6. Inventor's Oath or Declaration [Total Pages <u>2</u>] (including substitute statements under 37 CFR 1.64 and assignments serving as an oath or declaration under 37 CFR 1.63(e)) a. ☐ Newly executed (original or copy) b. ☒ A copy from a prior application (37 CFR 1.63(d)) 7. ☒ Application Data Sheet * See note below. See 37 CFR 1.76 (PTO/AIA/14 or equivalent) 8. CD-ROM or CD-R in duplicate, large table, or Computer Program (Appendix) ☐ Landscape Table on CD 9. Nucleotide and/or Amino Acid Sequence Submission (if applicable, items a. – c. are required) a. ☐ Computer Readable Form (CRF) b. ☐ Specification Sequence Listing on: i. ☐ CD-ROM or CD-R (2 copies); or ii. ☐ Paper c. ☐ Statements verifying identity of above copies	ACCOMPANYING APPLICATION PAPERS 10. ☐ Assignment Papers (cover sheet & document(s)) 11. ☐ 37 CFR 3.73(c) Statement ☐ Power of Attorney (when there is an assignee) 12. ☐ English Translation Document (if applicable) 13. ☐ Information Disclosure Statement (PTO/SB/08 or PTO-1449) ☐ Copies of citations attached 14. ☐ Preliminary Amendment 15. ☐ Return Receipt Postcard (MPEP § 503) (Should be specifically itemized) 16. ☐ Certified Copy of Priority Document(s) (if foreign priority is claimed) 17. ☐ Nonpublication Request Under 35 U.S.C. 122(b)(2)(B)(i). Applicant must attach form PTO/SB/35 or equivalent. 18. ☒ Other: CERTIFICATION AND REQUEST FOR PRIORITIZED EXAMINATION UNDER 37 CFR 1.102(e)
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***Note:** (1) Benefit claims under 37 CFR 1.78 and foreign priority claims under 1.55 **must** be included in an Application Data Sheet (ADS).
 (2) For applications filed under 35 U.S.C. 111, the application must contain an ADS specifying the applicant if the applicant is an assignee, person to whom the inventor is under an obligation to assign, or person who otherwise shows sufficient proprietary interest in the matter. See 37 CFR 1.46(b).

19. CORRESPONDENCE ADDRESS			
☒ The address associated with Customer Number: <u>58249</u> OR ☐ Correspondence address below			
Name			
Address			
City	State	Zip Code	
Country	Telephone	Email	
Signature	/Chun L. Yu/		Date October 25, 2021
Name (Print/Type)	Chun L. Yu, Ph.D.		Registration No. (Attorney/Agent) 68,138

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4). Dated: October 25, 2021 Electronic Signature for Chun L. Yu, Ph.D.: /Chun L. Yu/	
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258715898
258715898 v1

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	OSHH-001/C05US
		Application Number	
Title of Invention	BIOLOGICAL COLLECTION SYSTEM		
The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76. This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.			

Secrecy Order 37 CFR 5.2:

☐	Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)
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Inventor Information:

Inventor	1				Remove
Legal Name					
Prefix	Given Name	Middle Name	Family Name	Suffix	
	Youssef		BIADILLAH		
Residence Information (Select One) ☒ US Residency ☐ Non US Residency ☐ Active US Military Service					
City	Geneva		Country of Residence ⁱ	CH	
Mailing Address of Inventor:					
Address 1		Lamartine 14			
Address 2					
City	Geneva		State/Province		
Postal Code	CH-1203		Country ⁱ	CH	
Inventor	2				Remove
Legal Name					
Prefix	Given Name	Middle Name	Family Name	Suffix	
	Stephen	D.	ANDREWS		
Residence Information (Select One) ☒ US Residency ☐ Non US Residency ☐ Active US Military Service					
City	Falmouth	State/Province	ME	Country of Residence ⁱ	US
Mailing Address of Inventor:					
Address 1		11 Heron Point Road			
Address 2					
City	Falmouth		State/Province	ME	
Postal Code	04105		Country ⁱ	US	
All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the Add button.					
Add					

Correspondence Information:

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	OSHH-001/C05US	
		Application Number		
Title of Invention	BIOLOGICAL COLLECTION SYSTEM			

Enter either Customer Number or complete the Correspondence Information section below.
For further information see 37 CFR 1.33(a).

☐ An Address is being provided for the correspondence information of this application.

Customer Number	58249		
Email Address	zIPPatentDocketingMailboxUS@Cooley.com	Add Email	Remove Email

Application Information:

Title of the Invention	BIOLOGICAL COLLECTION SYSTEM		
Attorney Docket Number	OSHH-001/C05US	Small Entity Status Claimed	☐
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	9	Suggested Figure for Publication (if any)	

Filing By Reference:

Only complete this section when filing an application by reference under 35 U.S.C. 111(c) and 37 CFR 1.57(a). Do not complete this section if application papers including a specification and any drawings are being filed. Any domestic benefit or foreign priority information must be provided in the appropriate section(s) below (i.e., "Domestic Benefit/National Stage Information" and "Foreign Priority Information").

For the purposes of a filing date under 37 CFR 1.53(b), the description and any drawings of the present application are replaced by this reference to the previously filed application, subject to conditions and requirements of 37 CFR 1.57(a).

Application number of the previously filed application	Filing date (YYYY-MM-DD)	Intellectual Property Authority or Country

Publication Information:

☒ Request Early Publication (Fee required at time of Request 37 CFR 1.219)

☐ **Request Not to Publish.** I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application **has not and will not** be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32). Either enter Customer Number or complete the Representative Name section below. If both sections are completed the customer Number will be used for the Representative Information during processing.

Please Select One:	☒ Customer Number	☐ US Patent Practitioner	☐ Limited Recognition (37 CFR 11.9)
Customer Number	58249		

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	OSHH-001/C05US
		Application Number	
Title of Invention	BIOLOGICAL COLLECTION SYSTEM		

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, 365(c), or 386(c) or indicate National Stage entry from a PCT application. Providing benefit claim information in the Application Data Sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78.

When referring to the current application, please leave the "Application Number" field blank.

Prior Application Status		Pending		Remove	
Application Number	Continuity Type		Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)	
	Continuation of		16/023772	2018-06-29	
Prior Application Status		Abandoned		Remove	
Application Number	Continuity Type		Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)	
16/023772	Continuation of		15/227693	2016-08-03	
Prior Application Status		Patented		Remove	
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
15/227693	Continuation of	14/127832	2013-12-19	9442046	2016-09-13
Prior Application Status		Expired		Remove	
Application Number	Continuity Type		Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)	
14/127832	a 371 of international		PCT/US2012/043176	2012-06-19	
Prior Application Status		Expired		Remove	
Application Number	Continuity Type		Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)	
PCT/US2012/043176	Claims benefit of provisional		61/598601	2012-02-14	
Prior Application Status		Expired		Remove	
Application Number	Continuity Type		Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)	
PCT/US2012/043176	Claims benefit of provisional		61/598618	2012-02-14	
Prior Application Status		Expired		Remove	
Application Number	Continuity Type		Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)	
PCT/US2012/043176	Claims benefit of provisional		61/498584	2011-06-19	
Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the Add button. Add					

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Application Data Sheet 37 CFR 1.76		Attorney Docket Number	OSHH-001/C05US
		Application Number	
Title of Invention	BIOLOGICAL COLLECTION SYSTEM		

Foreign Priority Information:

This section allows for the applicant to claim priority to a foreign application. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55. When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX)ⁱ the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(i)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

Application Number	Country ⁱ	Filing Date (YYYY-MM-DD)	Access Code ⁱ (if applicable)	Remove

Additional Foreign Priority Data may be generated within this form by selecting the **Add** button.

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications

☐ This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013.

NOTE: By providing this statement under 37 CFR 1.55 or 1.78, this application, with a filing date on or after March 16, 2013, will be examined under the first inventor to file provisions of the AIA.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	OSHH-001/C05US
		Application Number	
Title of Invention	BIOLOGICAL COLLECTION SYSTEM		

Authorization or Opt-Out of Authorization to Permit Access:

When this Application Data Sheet is properly signed and filed with the application, applicant has provided written authority to permit a participating foreign intellectual property (IP) office access to the instant application-as-filed (see paragraph A in subsection 1 below) and the European Patent Office (EPO) access to any search results from the instant application (see paragraph B in subsection 1 below).

Should applicant choose not to provide an authorization identified in subsection 1 below, applicant **must opt-out** of the authorization by checking the corresponding box A or B or both in subsection 2 below.

NOTE: This section of the Application Data Sheet is **ONLY** reviewed and processed with the **INITIAL** filing of an application. After the initial filing of an application, an Application Data Sheet cannot be used to provide or rescind authorization for access by a foreign IP office(s). Instead, Form PTO/SB/39 or PTO/SB/69 must be used as appropriate.

1. Authorization to Permit Access by a Foreign Intellectual Property Office(s)

A. Priority Document Exchange (PDX) - Unless box A in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the State Intellectual Property Office of the People's Republic of China (SIPO), the World Intellectual Property Organization (WIPO), and any other foreign intellectual property office participating with the USPTO in a bilateral or multilateral priority document exchange agreement in which a foreign application claiming priority to the instant patent application is filed, access to: (1) the instant patent application-as-filed and its related bibliographic data, (2) any foreign or domestic application to which priority or benefit is claimed by the instant application and its related bibliographic data, and (3) the date of filing of this Authorization. See 37 CFR 1.14(h)(1).

B. Search Results from U.S. Application to EPO - Unless box B in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the EPO access to the bibliographic data and search results from the instant patent application when a European patent application claiming priority to the instant patent application is filed. See 37 CFR 1.14(h)(2).

The applicant is reminded that the EPO's Rule 141(1) EPC (European Patent Convention) requires applicants to submit a copy of search results from the instant application without delay in a European patent application that claims priority to the instant application.

2. Opt-Out of Authorizations to Permit Access by a Foreign Intellectual Property Office(s)

☐ A. Applicant **DOES NOT** authorize the USPTO to permit a participating foreign IP office access to the instant application-as-filed. If this box is checked, the USPTO will not be providing a participating foreign IP office with any documents and information identified in subsection 1A above.

☐ B. Applicant **DOES NOT** authorize the USPTO to transmit to the EPO any search results from the instant patent application. If this box is checked, the USPTO will not be providing the EPO with search results from the instant application.

NOTE: Once the application has published or is otherwise publicly available, the USPTO may provide access to the application in accordance with 37 CFR 1.14.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	OSHH-001/C05US
		Application Number	
Title of Invention	BIOLOGICAL COLLECTION SYSTEM		

Applicant Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.			
Applicant	1	Remove	
If the applicant is the inventor (or the remaining joint inventor or inventors under 37 CFR 1.45), this section should not be completed. The information to be provided in this section is the name and address of the legal representative who is the applicant under 37 CFR 1.43; or the name and address of the assignee, person to whom the inventor is under an obligation to assign the invention, or person who otherwise shows sufficient proprietary interest in the matter who is the applicant under 37 CFR 1.46. If the applicant is an applicant under 37 CFR 1.46 (assignee, person to whom the inventor is obligated to assign, or person who otherwise shows sufficient proprietary interest) together with one or more joint inventors, then the joint inventor or inventors who are also the applicant should be identified in this section.			
Clear			
☒ Assignee		☐ Legal Representative under 35 U.S.C. 117	
☐ Person to whom the inventor is obligated to assign.		☐ Person who shows sufficient proprietary interest	
If applicant is the legal representative, indicate the authority to file the patent application, the inventor is:			
Name of the Deceased or Legally Incapacitated Inventor: 			
If the Applicant is an Organization check here. ☒			
Organization Name		DNA GENOTEK, INC.	
Mailing Address Information For Applicant:			
Address 1		3000-500 Palladium Drive	
Address 2			
City		Ottawa	State/Province
Country		CA	Postal Code
Phone Number			Fax Number
Email Address			
Additional Applicant Data may be generated within this form by selecting the Add button. Add 			

Assignee Information including Non-Applicant Assignee Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

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Application Data Sheet 37 CFR 1.76		Attorney Docket Number	OSHH-001/C05US
		Application Number	
Title of Invention	BIOLOGICAL COLLECTION SYSTEM		

Assignee	1		
Complete this section if assignee information, including non-applicant assignee information, is desired to be included on the patent application publication. An assignee-applicant identified in the "Applicant Information" section will appear on the patent application publication as an applicant. For an assignee-applicant, complete this section only if identification as an assignee is also desired on the patent application publication.			
Remove			
If the Assignee or Non-Applicant Assignee is an Organization check here. ☒			
Organization Name	DNA GENOTEK, INC.		
Mailing Address Information For Assignee including Non-Applicant Assignee:			
Address 1	3000-500 Palladium Drive		
Address 2			
City	Ottawa	State/Province	ON
Country ⁱ	CA	Postal Code	K2V 1C2
Phone Number		Fax Number	
Email Address			
Additional Assignee or Non-Applicant Assignee Data may be generated within this form by selecting the Add button. Add			

Signature:[Remove](#)

NOTE: This Application Data Sheet must be signed in accordance with 37 CFR 1.33(b). However, if this Application Data Sheet is submitted with the **INITIAL** filing of the application and either box A or B is **not** checked in subsection 2 of the "Authorization or Opt-Out of Authorization to Permit Access" section, then this form must also be signed in accordance with 37 CFR 1.14(c).

This Application Data Sheet **must** be signed by a patent practitioner if one or more of the applicants is a **juristic entity** (e.g., corporation or association). If the applicant is two or more joint inventors, this form must be signed by a patent practitioner, **all** joint inventors who are the applicant, or one or more joint inventor-applicants who have been given power of attorney (e.g., see USPTO Form PTO/AIA/81) on behalf of **all** joint inventor-applicants.

See 37 CFR 1.4(d) for the manner of making signatures and certifications.

Signature	/Chun L. Yu/		Date (YYYY-MM-DD)	2021-10-25
First Name	Chun	Last Name	Yu	Registration Number
				68,138
Additional Signature may be generated within this form by selecting the Add button.				Add

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	OSHH-001/C05US
		Application Number	
Title of Invention	BIOLOGICAL COLLECTION SYSTEM		

This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Patent Application Fee Transmittal				
Application Number:				
Filing Date:				
Title of Invention:		BIOLOGICAL COLLECTION SYSTEM		
First Named Inventor/Applicant Name:		Youssef BIADILLAH		
Filer:		Chun L. Yu/Lucille Bonilla		
Attorney Docket Number:		OSHH-001C05US		
Filed as Large Entity				
Filing Fees for Track I Prioritized Examination - Nonprovisional Application under 35 USC 111(a)				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
UTILITY APPLICATION FILING	1011	1	320	320
UTILITY SEARCH FEE	1111	1	700	700
UTILITY EXAMINATION FEE	1311	1	800	800
REQUEST FOR PRIORITIZED EXAMINATION	1817	1	4200	4200
Pages:				
Claims:				
Miscellaneous-Filing:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
PUBL. FEE- EARLY, VOLUNTARY, OR NORMAL	1504	1	0	0
PROCESSING FEE, EXCEPT PROV. APPLS.	1830	1	140	140
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
Total in USD (\$)				6160

Electronic Acknowledgement Receipt	
EFS ID:	44116954
Application Number:	17510003
International Application Number:	
Confirmation Number:	3950
Title of Invention:	BIOLOGICAL COLLECTION SYSTEM
First Named Inventor/Applicant Name:	Youssef BIADILLAH
Customer Number:	58249
Filer:	Chun L. Yu/Lucille Bonilla
Filer Authorized By:	Chun L. Yu
Attorney Docket Number:	OSHH-001C05US
Receipt Date:	25-OCT-2021
Filing Date:	
Time Stamp:	17:55:37
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	DA
Payment was successfully received in RAM	\$6160
RAM confirmation Number	E202100H55504971
Deposit Account	
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:	

File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		OSHH-001_C05US-SPECIFICATION.pdf	316685	yes	36
			ca5958e5f73150f0206257a03f9ba3384d3fa571		
	Multipart Description/PDF files in .zip description				
	Document Description		Start		End
	Specification		1		30
	Claims		31		35
	Abstract		36		36
Warnings:					
Information:					
2	Drawings-only black and white line drawings	OSHH-001_C05US_DRAWINGS.pdf	919786	no	9
			4bd2a76d38be17139660905d032547ae2c9a3f9f		
Warnings:					
Information:					
3	Oath or Declaration filed	OSHH_001_C05US_DECLARATION.pdf	651275	no	2
			16c4e60e06d1608624d40a2f3732f796c977c23		
Warnings:					
Information:					
4	TrackOne Request	OSHH_001_C05US_Certification_and_Request_Track_One.pdf	164324	no	1
			3beeaa1e2275c816aa7dedd8c98863704cc27fd84		
Warnings:					
Information:					
5	Transmittal of New Application	OSHH_001_C05US_Transmittal.pdf	150825	no	1
			a05e72a53743e4750534703a48184a06bf6728ab		

Warnings:					
Information:					
6	Application Data Sheet	OSHH_001_C05US_Application _Data_Sheet.pdf	1256444	no	9
			de2f4ed4c9d4072a182cdb146dbaa14176e c5b3a		
Warnings:					
Information:					
7	Fee Worksheet (SB06)	fee-info.pdf	50601	no	2
			e8d8f646ad8f6912afdf102b46e681a22aa51 3b40		
Warnings:					
Information:					
Total Files Size (in bytes):			3509940		
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BIOLOGICAL COLLECTION SYSTEM

RELATED APPLICATIONS

[001] This application is a continuation of U.S. Patent Application No. 16/023,772, filed June 29, 2018, which is a continuation of U.S. Patent Application No. 15/227,693, filed August 3, 2016, which is a continuation of U.S. Patent Application No. 14/127,832, filed December 19, 2013, now U.S. Patent No. 9,442,046, which is a 35 U.S.C. § 371 national stage entry of PCT/US2012/043176, filed June 19, 2012, and claims priority under 35 USC §119(e) to U.S. provisional patent application nos. 61/498,584, filed June 19, 2011, 61/598,601, filed February 14, 2012, and 61/598,618, filed February 14, 2012. Each disclosure of the foregoing is herein incorporated by reference in its entirety.

Field of the Disclosure

[002] The disclosure relates to devices, solutions and methods for collecting samples of bodily fluids or other substances, including hazardous and/or toxic substances, and in particular, a naturally expressed bodily fluid (e.g., saliva, urine). In addition, the disclosure relates generally to functional genomics and to the isolation and preservation of cells from such bodily fluids, for studies in any of: functional genomic and epigenetic studies, and biomarker discovery (for example).

Background

[003] Personalized medicine is the customization of treatment to an individual as opposed to the one treatment-for-all model. Personalized medicine involves categorizing a patient based on his or her physical condition and designing an optimal healthcare solution exclusively for that category. The progression of personalized medicine is dependent on the discovery, validation, and commercialization of biomarkers to stratify populations for treatment and for the development of diagnostics for screening and early detection.

[004] Epigenetic research has come to the forefront of medical research and is implicated in the etiology of a number of physical and mental illnesses including: cancer, obesity, diabetes, schizophrenia, and Alzheimer's disease (Alika *et al.*, 2010; Grant *et al.* 2010; McGowen *et al.*,

2009; McGowen and Szyf, 2010; Plazas-Mayorca and Vrana, 2011; and Portela and Esteller, 2010). In addition, Epigenetics may hold particular promise in the many scientific and medical areas including but not limited to: cancer, diabetes, drug integrations, drug effectiveness, childhood aggression, suicidal behaviors, aging, inflammation, pain, obesity, schizophrenia, and other mental illnesses (Abdolmaleky et al., 2005; Costa et al., 2003; Iwamoto & Kato, 2009; Kuratomi et al., 2007; McGowan & Kato, 2007; McGowen and Szyf, 2010; Peedicayil, 2007; Petronis et al., 1999; McGowen and Szyf, 2010; Plazas-Mayorca and Vrana, 2011; and Zawia et al., 2009).

[005] A major challenge in the field includes the identification of an appropriate source material for home-based sample collection that is adequate for large-scale epigenetic research including whole-genome-analysis studies. Epigenetics may be the key for understanding the mechanisms of gene-environment interactions as growing evidence suggests that epigenetic mechanisms may provide a molecular memory of environmental experiences (Ho, 2010; Kappeler and Meaney, 2010; McGowen *et al.*, 2009, McGowen and Szyf, 2010; Portela and Esteller, 2010; Richards, 2008; Russo *et al.*, 2010; Tsai *et al.*, 2010; and Vlaanderen *et al.*, 2010). Preliminary data from some humans suggest that distinct methylation patterns in peripheral blood cells are associated with social behaviors including: childhood aggression, suicidal behaviors, and ageing (Kappeler and Meaney, 2010; McGowen *et al.*, 2009; McGowen and Szyf, 2010; Portela and Esteller, 2010; Russo *et al.*, 2010, Tierling *et al.*, 2010; Tsai *et al.*, 2010; and Zhang et al., 2011).

[006] Due at least in part to the heterogeneous nature of human disease, particularly mental illness, and the complex interaction of contributing etiological factors, studies require large sample sizes to provide reliable and significant effects. However, current research options for sample collection for epigenetic studies do not meet this requirement of “large sample sizes.” The need for large sample sizes for studies is also true in order to produce significant effects in regards to studying human-environment interactions as these interactions are also of a very complex nature with many contributing factors. The ability to perform large-scale “population sized” (subject samples numbering in at least the hundreds to thousands) epigenetic research can introduce a new understanding of human-environment interaction and facilitate the completion of longitudinal studies facilitating the development of epigenetic-based screening diagnostics crucial to the progression of modern medicine. This epigenetic research may lead to a new understanding of how the environment affects our epigenome and how this relates to a person’s health outcome, which may further lead to the development of preventative

interventions for individuals who are considered high-risk and diagnostics for these health disparities including, but not limited to, diagnosis.

[007] Some epigenetic studies attempting to quantify environmental and other complex interactions in human populations use blood as the source material for experimentation. Blood can restrict the researcher's ability to conduct large population-sized studies as it:

1. generally requires medical supervision,
2. involves invasive procedures for collection,
3. carries stigma that limits participation, and
4. is expensive to collect and ship.

[008] Naturally expressed bodily fluids, e.g., saliva and urine, can be an additional or alternative appropriate source material for home-based sample collection as they:

1. do not require invasive techniques,
2. do not have the same stigma as blood,
3. do not require professional supervision, and
4. can be inexpensive to collect.

[009] In addition, at least saliva has been shown to contain white blood cells (Dos-Santos et al., 2009). The use of bodily fluids, e.g., saliva, urine, may enable large-scale "population-sized" epigenetic research. In addition, home-base sample collection of saliva, or urine, may allow for a much wider range of research options available as it can greatly increase participant numbers and samples can be more easily shipped by the subjects from anywhere in the world. For example, the ability to more easily ship samples from anywhere in the world can be particularly useful when samples are from countries that do not have laboratory infrastructure.

[0010] An organism's genome is a fixed sequence that contains its hereditary information and is the same in every cell of an organism. An organism's epigenome, by contrast, varies between cell types and changes over the organism's lifetime. Thus, epigenetic studies may include a single cell type as the source of sample material to control for these differences (Johnson and Tricker, 2010; Lister *et al.*, 2009; and Rangwala *et al.*, 2006). For example, human saliva contains numerous cell types, including epithelial cells, cells normally found in the blood (i.e., T-cells and B-cells), bacteria and debris (Dos-Santos *et al.*, 2009 and Viet and Schmidt, 2008). The cells in saliva that are the most important to profile epigenetically are

those that come from the blood stream, as these cells carry epigenetic information from the entire body (Kappeler and Meaney, 2010; McGowen and Szyf, 2010; McGowen and Szyf, 2010; Righini *et al.*, 2007; Rosas *et al.*, 2011, Vlaanderen *et al.*, 2010 and Zhang *et al.*, 2011).

[0011] Additionally, it may not be practical to use whole saliva DNA as the cells in saliva that are not found in the blood, such as epithelial cells, which make up the vast majority of cells in saliva (Dos-Santos *et al.*, 2009) have the ability to “mask” the epigenetic effects seen in T-cells (cells that originated in the blood) by dampening the effect of the minority of cells (Dos Santos *et al.*, 2009, Lister *et al.*, 2009; and Tierling *et al.*, 2010). To address these concerns AboGen developed a method to separate and extract the different cell types found in bodily fluids such as saliva by taking advantage of cell-specific markers and isolation techniques (e.g., magnetic). This method uses practical amounts of bodily fluids, such as saliva, to yield enriched cells that can be used for downstream biological applications including large-scale functional genomic studies (example epigenomic studies). For example, saliva sample processing technology allows collected samples to be processed into single cell types and have their epigenomes profiled.

[0012] Furthermore, saliva (and other bodily fluids) can present challenges with cell isolation as a source material for blood cells in respect to downstream experimentation for reasons such as:

1. Blood is a transporter fluid while saliva is a digestive fluid that can be rich in proteases, enzymes and secreted substances and urine is a excretory fluid consisting of unwanted waste products.
2. Some fluids can have a wide pH range and some of the pH values reported, such as for saliva, would result in death if blood reached that pH (saliva is 6.2-7.4; urine is 4.5-8; blood is 7.35-7.45).
3. Some fluids contain more bacteria than blood.
4. Some fluids contain non-cellular material that varies between individuals and interferes with cell isolation.
5. Some fluids include blood cells, such as T-cells, which can be abundant in blood, but may be rare in

other naturally expressed bodily fluids, such as saliva or urine, and are vastly outnumbered by other cell types, such as epithelial cells, unlike in blood.

6. The subset of lymphocyte cells in some bodily fluids, such as saliva, greatly differs from the population of those cell types in blood. For example, only CD4+CD8- T-cells are reported to be found in saliva.
7. Some fluids are produced each day, such as saliva at about a rate of .5- 1.5 liters per day per person.

[0013] Therefore, there is a need for new methods for isolating rare cells (i.e., T-cells) from saliva and other naturally expressed bodily fluids.

[0014] For collecting saliva samples from a large population of people (example: functional genomic studies) who are widely geographically dispersed, several requirements may need to be met for an optimal sample collection device. For example, it may be beneficial to have the sample collection device securely house a toxic preservative solution in a closed chamber. Additionally, the sample collection device may be able to be sent to a donor with the toxic solution safely enclosed. The sample collection device may also allow easy and safe collection of a donor specimen, such as human saliva or urine, with no risk of exposure of the donor to the toxic solution. Furthermore, the sample collection device may allow the donor to safely mix the toxic solution and the specimen (for preservation of the specimen) with no risk of exposure of the donor to neither the toxic solution nor any other hazard. The sample collection device may also allow the donor to send the sample collection device to a laboratory for processing generally “as-is” after securely closing the sample collection device. Finally, the sample collection device may further allow a laboratory technician to receive the sample collection device and safely open it for processing with generally no risk of exposure to any hazards.

[0015] Some currently available sample collection devices include, for example, US patent no. 7,482,116 which describes a device that utilizes disassociating a barrier to allow fluid communication between a cavity holding the donor sample and a solution, however, embodiments included in the patent are limited to the use of sharp extruding objects and thin pierceable membranes. The thin pierceable membranes can represent a safety hazard to the sample donor as any wrong manipulation (such as with a finger nail) can lead to piercing of

the membrane and release of the solution. US patent publication no. 2009/0216213 A1 claims a device that utilizes a pierceable membrane to establish fluid communication between a cavity containing a solution and the donor sample. This can represent a safety hazard to the sample donor as any wrong manipulation can lead to piercing the membrane and exposing the solution. The device also requires exchange of the cap prior to sending the sample to the end user. This can represent a safety hazard as it may expose the sample donor to the potentially toxic solution. Therefore, there is a need for safer and easier to use sample collection devices.

[0016] Additionally, the purification process requires cells to maintain their antigen profiles and the epigenomic profiling requires that their epigenome be maintained. To this end, it is necessary to treat the cells in such a way that they are able to generally maintain these features. Currently available treatments generally do not meet this need. For example, US Patents 7,267,980 and 7,749,757 disclose solutions containing lysine, glycine and formaldehyde for stabilizing cells from blood. However, those solutions will not protect cells from proteases found in some bodily fluids, such as saliva. Therefore, there is a need for new solutions and methods that will preserve the antigenicity and epigenome of cells in other bodily fluids, such as saliva.

SUMMARY OF THE DISCLOSURE

[0017] Embodiments of the disclosure provide safer and easy to use sample collection devices for naturally expressed bodily fluids (for example), as well as solutions and methods for preserving cells of samples collected, and additionally, methods for isolating specific cells either collected and/or preserved. Such isolated cells (and even non-isolated collected cells), can then be analyzed for studies in any of: functional genomic and epigenetic studies, and biomarker discovery (for example).

[0018] The sample collection devices according to the present disclosure provide several advantages over currently available sample collection devices. For example, in some embodiments, the sample collection devices use a minimum amount of parts and do not require removal or exchange of a piece or an object thereof. In some embodiments, the sample collection devices do not require any additional manipulation by the sample donor apart from depositing the sample in the sample collection device and closing the sample collection device. In some embodiments, use of the sample collection devices provide improved safety for both the sample donor and the end user, since, for example, sharp objects are not included and there

is limited to no risk of exposure to toxic solutions (e.g., sample preservative solutions).

[0019] In some embodiments of the sample collection device, the sample collection device can have two main mating bodies, a cap and a tube. The cap can include a closed cavity holding a preservative solution which can mate with the tube to constitute the closed sample collection device. The tube can be configured to receive the donor specimen. The cap and tube are configured so that when the donor deposits the specimen and closes the tube with the cap, the cavity holding the preservative solution may be opened to release the preservative solution and allow it to mix with the donor specimen.

[0020] In some embodiments, a bodily fluid sample collection device for the collection of naturally expressed bodily fluids is provided and includes a cap having an outer wall having an engagement member, and an interior chamber for holding a fluid. The chamber may comprise inner walls which define an interior space and an aperture, where the aperture is configured for sealing by a removable blocking member. The blocking member may include a first coupling member for engaging a corresponding second coupling member in a tube, thereby causing removal of the blocking member and opening of the aperture when the cap is coupled to the tube. The device also includes the tube which includes a containment wall defining a reservoir for bodily fluid sample collection, an engagement member complementary to the engagement member of the cap, and the second coupling member.

[0021] In some embodiments, one and/or another of the following features may be provided with a sample collection device:

- the removable blocking member is a disk-shaped member which threadably engages the aperture;
- the first coupling member comprises an indentation disposed centrally in the bottom of the blocking member and the second coupling member is disposed centrally within the tube;
- the first coupling member comprises a recess disposed eccentrically in the bottom of the blocking member and the second coupling member is disposed eccentrically within the tube;
- the removable blocking member comprises an annular member having threads arranged thereon, where the annular blocking member substantially covers the aperture, and the inner wall of the cap includes complementary threads, such

that the annular member can be screwed into the interior space to uncover the aperture;

- a locking mechanism, to lock the cap to the tube (or lock any two components together), the locking mechanism may comprise a wedge and a complementary flange;
- a sealing mechanism which may comprise a sealing substance associated with the engagement member of the cap, where upon coupling the cap to the tube, the sealing substance flows into at least the engagement member of the cap;
- tamper-evident means for determining whether the cap has been opened, which may comprise a ring having a first portion thereof integral with an open end of the cap, where upon the cap being coupled to the tube, the ring is positioned adjacent the tube; as such, in some embodiments, upon the cap being de-coupled from the tube, the first portion is broken and the ring remains substantially adjacent the tube; and/or
- the fluid in the cap chamber comprises a solution for preserving cells.

[0022] In some embodiments, a bodily fluid sample collection device for the collection of naturally expressed bodily fluid is provided and includes a cap having an interior chamber for holding a fluid and a first engagement member, and a tube comprising a containment wall defining a reservoir for sample collection and a second engagement member for engagement to the first engagement member. In some such embodiments, the cap comprises an outer wall having the first engagement member, the chamber comprises inner walls defining an interior space which holds the fluid, and an aperture, the aperture being configured for sealing by a removable blocking member. In addition, in some embodiments, the blocking member includes a first coupling member for engaging a corresponding second coupling member of the tube, where upon the coupling of the cap to the tube, the blocking member is moved and the aperture opens.

[0023] In some embodiments, a method for collecting a sample of a naturally expressed bodily fluid (or toxic or hazardous fluid) is provided and includes providing a bodily fluid collection device according to any of the disclosed sample collection device embodiments, depositing the bodily fluid into the chamber, and mating the cap and tube together such that the corresponding engagement members engage, where the blocking member moves and the preservation fluid flows into the reservoir containing the bodily fluid such that cells contained in the bodily fluid

are preserved for analysis. In some such embodiments, further steps may include at least one of (with reference to bodily fluids): isolating one or more cell types for a plurality of cell types in the bodily fluid, and analyzing the collected cells.

[0024] As one of skill in the art will appreciate, in some embodiments, at least one of DNA, RNA and proteins can be extracted from collected/preserved cells, whether the isolated cells, or non-isolated cells.

[0025] In some embodiments, a kit for the collection of naturally expressed bodily fluids (or toxic and/or hazardous fluids) is provided and comprises a plurality of sample collection devices according to of the disclosed sample collection devices.

[0026] In addition, the current disclosure relates to functional genomic studies including epigenetic studies. More particularly, this disclosure also relates to the isolation of cells from bodily fluids, such as saliva and urine, for these studies. Accordingly, some embodiments of the disclosure include methods for preserving the antigenicity and epigenome of cells, and isolating rare cells, including, without limitation T-cells from bodily fluids, such as saliva and urine, are disclosed herein.

[0027] As used herein, the collection of “bodily fluids” generally refers to the collection of naturally expressed bodily fluids (although some embodiments can be used for collection of intravenous collection methods – e.g., blood). Thus, with references to the disclosed embodiments, “bodily fluids” refer to naturally expressed bodily fluids including, for example, saliva and urine.

[0028] For example, in some embodiments, a solution for preserving cells in bodily fluids, such as saliva and urine, is provided for further separation into cell types and downstream analysis that allows for the cells in saliva to retain their antigenicity and cellular architecture during storage. The solution can contain at least one chemical fixing agent, such as but not limited to paraformaldehyde, and at least one protease inhibitor. In some embodiments, the solution may further contain, for example, one or more of: at least one antimicrobial agent, serum proteins from human and/or other animal species. The solution may be buffered at a pH between about 6.4 to about 8.4, and in some embodiments, between about 7.2 to about 7.6.

[0029] In some embodiments, a method for preserving cells in one or more bodily fluids includes contacting collected cells with a solution according to one and/or another embodiment of the present disclosure, which allows the cells to retain their antigenicity and epigenome, for example.

[0030] In some embodiments, a method for isolating cells from chemically fixed cells collected from a bodily fluid, e.g., saliva or urine, and includes centrifuging the cells to separate, for example, DNA and/or other soluble material from a pellet of cells, bacteria, and debris, enriching white blood cells from other contents of the pellet, and isolating specific cells (e.g., white blood cells) using antibodies conjugated to magnetic beads targeted to cell specific markers.

[0031] In some embodiments, methods for isolating a particular type of cell, for example, a type of white blood cell (e.g., lymphocytes), from one or more bodily fluids (e.g., saliva and/or urine), and includes one or more of the following steps (and, depending upon the embodiment, several or all of the following steps): providing a sample of bodily fluid comprising chemically fixed cells, optionally centrifuging the bodily fluid sample to obtain a pellet comprising cells, optionally re-suspending the pellet in a buffer, subjecting the re-suspended pellet to density gradient separation to obtain a layer of a mixture of white blood cell types (including lymphocytes), contacting the mixture of cell types with a solution containing specific binding agents for an epitope found on a particular type of white blood cell, and separating the particular type of white blood cell (including lymphocytes) from the mixture of white blood cell types.

[0032] In some embodiments, the specific binding agents may be magnetic beads coupled to antibodies specific to an epitope found on a particular type of white blood cell, and in the separation step may then comprise, for example, magnetically separating the particular type of white blood cell (including lymphocytes) from the mixture of white blood cell types (though other cell separation techniques are within the scope of the disclosure).

[0033] In some embodiments, the bodily fluid (e.g., saliva, urine) can be mixed with a chemical fixative solution and the mixture can be removed from the pellet. The pellet can then be re-suspended in a buffer. The re-suspended pellet may optionally be centrifuged and washed one or more times in the buffer. The washed pellet may then be applied to a hydrophilic polysaccharide mixture to form a gradient. This gradient may be different than that used for blood because the density of the cells in other bodily fluids (e.g., saliva, urine) after chemical fixation for preservation can be different due to the different density of the preserved cells requiring an alteration in the time, temperature, and/ or density of the gradient for the cells to be processed through this density gradient.

[0034] Additionally, in some embodiments, the white blood cells can form a layer in the

gradient. The white blood cell layer can be extracted from the gradient and placed in another centrifuge tube where it may be washed in a buffer and re-pelleted to remove the remaining gradient mixture. The pellet may then be re-suspended and incubated in a buffer containing antibodies that are conjugated to magnetic beads and specific to antigens that are specific for a cell type to be isolated. In some embodiments, the cell type to be isolated is T-cells and the antigen is a T-cell-specific antigen. In some embodiments, the antigen is CD4. The re-suspended cells in the buffer can be bound by the antibody and subjected to a magnetic field that magnetically attracts the cells bound to the antibody-conjugated magnetic beads to the side of the tube. Remaining liquid may then be removed from the tube and the tube is washed in buffer. Isolated T-cells then remain attracted to the side of the tube and are ready for further processing, such as freezing for later downstream experimentation (for example).

[0035] In some embodiments, a method for preserving cells in a naturally expressed bodily fluid comprises contacting the bodily fluid with the preservation solution according to any of the disclosed embodiments.

[0036] The devices, solutions and methods of sample collection, preservation, isolation and analysis will be better understood in light of the following drawings, detailed description and claims. Like reference symbols in the various drawings indicate like elements.

[0037] It is worth noting that while some embodiments of the sample collection devices disclosed herein are set forth for use with the collection of bodily fluids, the same also has particular use with the collection of any other substance, including hazardous and/or toxic fluids.

BRIEF DESCRIPTION OF THE DRAWINGS

[0038] FIG. 1 shows a sample collection device comprising a cap and a tube according to some embodiments of the present disclosure.

[0039] FIG. 1A is a cross section view taken along line 1A-1A of FIG. 1 and shows the interior chamber of the cap comprising inner walls which define an interior space and an aperture according to some embodiments of the present disclosure.

[0040] FIG. 1B is a cross section view taken along line 1B-1B of FIG. 1A and shows a coupling member centrally positioned within the tube according to some embodiments of the present disclosure.

[0041] FIG. 2A shows a longitudinal cross section view of a sample collection device in which

the cap contains an inner chamber with a removable blocking member that has an eccentrically located coupling feature which can mate with a coupling member eccentrically located in the tube according to some embodiments of the present disclosure.

[0042] FIG. 2B is a cross section view taken along line 2B-2B of FIG. 2A and shows a coupling member eccentrically positioned within the tube according to some embodiments of the present disclosure.

[0043] FIG. 3A shows an embodiment of the cap of the sample collection device in which the cap contains an inner chamber with a movable annular member that can cover an aperture in the inner wall according to some embodiments of the present disclosure.

[0044] FIG. 3B shows an embodiment of the sample collection device in which the cap is coupled to the tube and the movable annular member is moved to a position where it does not cover an aperture in the inner wall according to some embodiments of the present disclosure.

[0045] FIG. 3C is a top view of the tube shown in FIG. 2B and shows a coupling member positioned within the tube according to some embodiments of the present disclosure.

[0046] FIG. 4A shows an embodiment of the sample collection device comprising a locking mechanism disposed within the inside of the cap and the tube, which prevents the cap from being removed by at least the donor after the cap has been coupled to the tube according to some embodiments of the present disclosure.

[0047] FIG. 4B shows the locking mechanism in the sample collection device shown in FIG. 4A showing a locked configuration and an unlocked configuration according to some embodiments of the present disclosure.

[0048] FIG. 5A shows a sample collection device comprising a locking mechanism disposed on an outer surface of the cap and tube, which prevents the cap from being removed by at least the donor after the cap has been coupled to the tube according to some embodiments of the present disclosure.

[0049] FIG. 5B shows the locking mechanism in the sample collection device shown in FIG. 5A showing a locked configuration and an unlocked configuration according to some embodiments of the present disclosure.

[0050] FIG. 6 shows a sample collection device further including a sealed cavity containing a sealing solution that is released into the engagement features of the cap and tube when the cap is coupled to the tube, which prevents the cap from being removed by at least the donor after

the cap has been coupled to the tube according to some embodiments of the present disclosure.

[0051] FIG. 7A shows a “tamper-evident” cap, in which an annular member at the bottom of the cap can break away from the cap if the cap has been removed after having been rotated/screwed onto the tube according to some embodiments of the present disclosure.

[0052] FIG. 7B shows the “tamper-evident” cap shown in FIG. 7A showing the annular member broken away from the cap according to some embodiments of the present disclosure.

[0053] FIG. 8 shows the time course of DNA yield in samples stored in chemical fixative solution at room temperature after 0, 1, 2 and 7 days, as well as DNA extracted from T-cells from each sample according to some embodiments of the present disclosure.

[0054] FIG. 9 is a chart illustrating the relative yield of extracted T-cells per ml of starting material (e.g., sample of bodily fluid), as compared to a yield of T-cells from blood.

[0055] FIG. 10 shows a saliva dose curve of micrograms of isolated T-cell DNA per ml of saliva according to some embodiments of the present disclosure.

DETAILED DESCRIPTION OF THE EMBODIMENTS

[0056] Embodiments of the present disclosure include devices, solutions and methods for the collection of samples, such as bodily fluids, as well as methods for isolating one or more cell types from collected cells (chemically fixed or otherwise). For example, in some embodiments, the sample collection devices provide several advantages over currently available sample collection devices, and in addition, the sample collection devices according to some embodiments use a minimum amount of parts and the devices do not require removal or exchange of a piece or an object. Furthermore, in some embodiments, the sample collection devices may generally not require additional manipulation by the sample donor apart from depositing the sample and closing the collection device. The sample collection devices according to some embodiments include improved safety of use for both sample donors and end users due, at least in part, to the elimination of sharp objects and limited risk of exposure to toxic solutions, as will be described in greater detail below.

[0057] In some embodiments, methods for the preservation and isolation of cells from bodily fluids for functional genomic and epigenetic studies, as well as biomarker discovery, are provided. Additionally, this disclosure provides devices, solutions and methods for isolating rare preserved cells, such as T-cells, from bodily fluids (i.e., saliva, urine), as will also be

described in greater detail below.

[0058] Some embodiments of the sample collection device may include two mating bodies, such as a cap and a tube. In some embodiments, the cap may include a closed cavity, such as an interior space, for holding a preservative solution (which may be toxic) for mating with the tube to constitute a closed sample collection device. The tube may be configured to receive a donor specimen, such as one or more bodily fluids (e.g., saliva, urine). In some embodiments, the cap and/or tube may be configured so that when the donor deposits the specimen and closes the tube with the cap, the cavity in the cap, which may be holding the preservative solution, can be opened to release the preservative solution and allow it to mix with the donor specimen.

[0059] One of skill in the art will appreciate that with respect to some embodiments of the collection device described herein, such may be used in combination with accessories that ease specimen deposit within the collection device, including, for example, mouth adapters for saliva collection, funnels and hoses for urine collection, and the like.

[0060] In some embodiments, the sample collection device may comprise a cap having an outer wall with interior threads. Additionally, the sample collection device may include an interior chamber for holding a fluid with the chamber comprising walls defining an interior space and a threaded aperture in the wall. The aperture in the wall may be sealed by a threadably removable blocking member, where the blocking member may include engaging members for engaging a coupling member in a tube, thereby causing the blocking member to be removed and the aperture to open when the cap is threaded onto the tube (in some embodiments). In some embodiments, the sample collection device may further include a tube comprising a containment wall defining a lumen or reservoir for sample collection, exterior threads complementary to the interior threads of the outer wall of the cap, and a coupling member that has a shape which is complementary to the engaging member in the cap.

[0061] In some embodiments, the threadably removable blocking member can be a disk-shaped member that is at least one of pushed, rotated, screwed, threaded, and/or mated into the aperture of the inner chamber and can be at least one of pushed, rotated, screwed, threaded, and/or mated into the chamber by interaction between the engaging member of the cap and the coupling member of the tube when the cap is rotated or screwed onto the tube. The engaging member can be either centrally or eccentrically located in the disk-shaped member, with the coupling member being at least one of centrally or eccentrically located in the tube, respectively.

[0062] The terms push, rotate, screw, mate as well as thread, couple, and attach, as well as any corresponding tenses and plurals thereof (as additionally including the term “feature(s)), disclosed herein, correspond to structure (well known to those of skill in the art) for connection (either permanent or temporary) of two (or more) components (e.g., “screw means” “mating means”, “coupling feature”, “engagement feature”). For example, with respect to “pushing”, such means can cover a “snap-fit” type of structure; rotation means can cover means in which a protruding member is received by a corresponding recess when one component is rotated relative to another. “Screwed” and “threadably” covers helical threaded engagement and the like. Thus, use of any of these terms (or tenses thereof) can also cover such connection with any such means or the equivalents thereof.

[0063] In some embodiments, a threadably movable annular member may not fit into the aperture, but rather covers the aperture from the outside of the inner chamber. In such embodiments, the annular member can have interior threads complementary to threads on the outside of the inner chamber or interior space. Interaction between the coupling features of the annular blocking member and the coupling member of the tube can cause the annular member to be screwed up the outside of the inner chamber, away from the aperture.

[0064] In some embodiments, the sample collection device may further include locking or sealing means, such that the cap cannot be removed from the tube by the donor once the cap has been connected or screwed onto the tube, such as by the donor. Suitable locking members can include a wedge on the cap and a matching flange on the tube or visa-versa. The wedge and flange can either be on the inside of the cap and tube, or on the outside of the cap and tube. Suitable sealing means include a sealed cavity containing a sealing solution, such as a glue, wherein the sealing solution is released when the cap is pushed, rotated or screwed onto the tube and thereafter cures in order to prevent disengagement between the cap and tube. In some embodiments, the sealing solution may be a two-component glue, such as an epoxy, with one component being sealed into the cap, and the other component sealed into the tube, such that the two components mix within the threads when the cap is screwed onto the tube. In other embodiments, the sealing solution can be a single component, such as a cyanoacrylate-based glue, which can be in a sealed cavity in the cap or tube, such that the sealing solution is released into the threads when the cap is screwed onto the tube. In some embodiments, the sealing solution can cure soon after engagement between the cap and tube such that disengagement between the tube and cap by the user can be generally prevented.

[0065] Alternatively, or in addition, some embodiments may further include an annular

member at the base of the cap that is partially secured to the cap, such that removal of the cap after it has been screwed onto the tube breaks the bond between the cap and the annular member, thereby indicating that the tube has been opened. This “tamper-evident” embodiment is similar to those used to attach a cap to a soda bottle.

[0066] The sample collection devices according to some embodiments can be made of any suitable plastic, such as polypropylene, polystyrene and polycarbonate. The dimensions of the device can be modified to suit the specific processing the sample will be subjected to. In certain embodiments, typical dimensions include the following. For the inner chamber of the cap, the volume is from about 3 ml to about 10 ml, typically about 6 ml. For the lumen of the tube, the volume is from about 15 ml to about 50 ml, typically about 25 ml. Other volumes are within the scope of some embodiments of the present disclosure.

[0067] With respect to the figures, FIG. 1 is an illustration of an embodiment of a sample collection device 10 comprising a cap 12 and a tube 14. The tube can be configured for collection of one or more sample bodily fluids, and the cap can be configured for storing one or more preservation fluids. Additionally, the cap 12 and tube 14 can be configured to securely mate with one another in order to provide a secure containment of at least the sample bodily fluids for storing and shipping. Furthermore, the mechanism by which may be implemented in the sample collection device 10 for securely mating the cap 12 and the tube 14 may prevent disengagement between the cap 12 and the tube 14. One benefit of preventing disengagement between the cap 12 and the tube 14 is that it can prevent at least, for example, contamination of the sample contained in the tube and exposure of any preservation solutions (which may be toxic) to the sample donor, such as those contained in the cap 12.

[0068] FIG. 1A shows an example interior chamber 16 of the cap 12 which may be defined by at least one outer wall 24 and at least one inner wall 18 according to some embodiments. The at least one inner wall 18 may further define an interior space 20 and an aperture 22. In addition, the outer wall 24 may include one or more cap engagement features 34 along at least one side of the outer wall 24 for engaging the tube 14. For example, and shown in FIG. 1A, an inside surface 26 of the outer wall 24 can include one or more cap engagement features 34, such as threads, for engaging and mating with one or more complimentary tube engagement features 38, such as threads, associated with the tube 14. The tube 14 may be comprised of at least one containment wall 32 which may define a reservoir 40 for collecting and storing sample body fluids, such as saliva or urine. An outer surface 30 of the containment wall 32 may include the one or more tube engagement features 28, such as threads.

[0069] The cap 12 may further include an aperture 22 having one or more aperture engagement features 42, such as threads. In addition, the cap 12 may include a blocking member 46 which may have one or more blocking member engagement features 44, such as threads, for engaging the aperture engagement features 42. For example, the blocking member 46 may be removably coupled to the aperture 22 such that when the blocking member is secured to the aperture, one or more fluids or materials, may be contained within the interior space 20 of the cap. However, upon decoupling of the blocking member 46 to the aperture 22, the one or more fluids or materials may be released from the interior space 20 in the cap 12. For example, once the cap 12 has at least been partially secured to the tube 14, the blocking member 46 may be decoupled from the aperture 22, thereafter allowing fluids or materials in the interior space 20 to be released into the reservoir 40 of the tube 14. The one or more fluids or materials contained in the interior space 20 in the cap 12 may assist in preserving the sample body fluids contained in the reservoir 40 of the tube 14 during at least storage and shipping. Any of the engagement features discussed herein may be any number of engagement features for allowing temporary or permanent engagement between two parts or features of the sample collection device 10 and are not limited to the examples discussed in this disclosure.

[0070] The blocking member 46 may also include one or more coupling features 48 which may allow one or more coupling members 50 comprising a part of the tube 14 to engage and couple with the coupling features 48. The coupling between the coupling features 48 and coupling members 50 can assist in decoupling the blocking member 46 from the aperture 22. For example, as the cap 12 is secured to the tube 14, the coupling member 50 may engage and interact with the coupling feature 48 of the blocking member 46, such as similar to the head of a screw driver interacting with the head of a screw. The blocking member 46 may be threadably engaged with threaded aperture engagement features, and the coupling and interaction of the coupling feature 48 and coupling member 50 may cause the threaded engagement between the blocking member 46 and the aperture 22 to be released. The threaded engagement between the blocking member 46 and the aperture 22 may be released, for example, due to rotation of the blocking member 46 relative to the aperture 22. Any number of releasable engagements may be used to engage the blocking member 46 with the aperture 22 such that the engagement between the blocking member 46 and the aperture 22 may be released upon securing the cap to the tube 14. Similarly, any number of features may be integrated in the sample collection device 10 which may allow containment of a solution in a part of the cap 12 or tube 14 such that the solution is not released until the cap is at least

partially secured to the tube 14.

[0071] The tube 14 in FIG. 1A is shown by way of example as having a coupling member 50 in the shape of a square peg which is complementary to a square shaped indent comprising the coupling feature 48 in the blocking member 46. Furthermore, the coupling member 50 can be centrally located within the tube 14 and the coupling feature may be centrally located on the bottom of the blocking member 46. Therefore, upon threaded engagement between the cap 12 and the tube 14, the square peg coupling member 50 may extend into and engage the square shaped indent coupling feature 48 in the blocking member 46, thus preventing the blocking member 46 from rotating relative to the coupling member 50. However, although the blocking member 46 may be prevented from rotating relative to the coupling member 50, the blocking member 46 may rotate relative to the aperture 22 and become disengaged from the aperture 22, such as from releasing the threaded engagement between the blocking member 46 and aperture 22. FIG. 1B shows an example coupling member 50 secured to an inner surface 52 of the containment wall of the tube 14 by more than one cross-member 54. The one or more cross members 54 can assist in securing the position of the coupling member 50 while allowing space for the passage of fluids or materials into the reservoir 40.

[0072] An example method of use of a sample collection device 10 can include the sample collection device 10 supplied with sample preservation fluid in the interior space 20 of the cap 12, and with the blocking member 46 threadably engaged with the aperture 22 in order to contain the sample preservation fluid in the interior space 20. Sample fluid, such as saliva or urine, may then be placed in the reservoir 40 of the tube 14 by a donor. The cap 12 can then be screwed onto the tube 14. Screwing the cap 12 onto the tube 14 may cause the coupling member 50 in the tube 14 to engage the coupling feature 48 of the blocking member 46 and unscrew the blocking member 48 from the aperture 22 and into the interior space 20 of the cap 12. Decoupling the blocking member 48 from the aperture 22 can allow the sample preservation fluid to flow into the reservoir 40 of the tube 40. After release of the sample preservation fluid into the reservoir 40 of the tube 14, the sample preservation fluid can mix with the donor's sample fluid, thereby preserving the donor's sample fluid.

[0073] While shown as a square peg in this illustration, the coupling member 50 of the tube 14 can be any shape that is complementary in shape with the coupling feature 48 of the blocking member 46 such that it allows the blocking member 46 to decouple from the aperture 22. The coupling feature 48 can be either in the blocking member 46 or the tube 14, and the complimentary coupling member 50 may be either in the tube 14 or blocking member 46,

respectively. Other shapes will be evident to one skilled in the art, including, without limitation, a slot and a tab, like a regular screwdriver and screw, or a cross-shaped pair, like a Phillips screwdriver and screw.

[0074] An additional embodiment of the sample collection device 100 is shown by way of example in FIGS 2A and 2B. The sample collection device 100 may include one or more coupling members 50 and complimentary coupling feature 48 which may be placed eccentrically from either the cap 12 or tube 14. As shown in FIG. 2B, less material and parts may be required for this embodiment to work properly, such as the coupling member 50 maintaining proper positioning by only one cross-member 54. Although the coupling member 50 is shown as being held in position by only one cross-member 54 extending from the containment wall 32 of the tube 14, any number of configurations and cross-members 54 may be used to position the coupling member 50 without departing from the scope of this disclosure.

[0075] Another embodiment of the sample collection device 200 is shown by way of example in FIGS 3A-3C. More specifically, FIG. 3A shows a cross section of the cap 12 prior to being coupled to the tube 14. The cap 12 can include an outer wall 24 and cap engaging members 34 along an inside surface 26 of the outer wall 24. The interior space 20 may be at least partially defined by at least one of an inner wall 18 or outer wall 24 of the cap 12. Furthermore, the inner wall 18 can include engagement features 60, such as threads, along a surface of the inner wall 18. The inner wall 18 may further define an aperture 22 which may be open or closed depending on the position of an annular blocking member 62 relative to the aperture 22. When the aperture 22 is closed such that the annular blocking member 62 is covering the aperture 22, fluid or material, such as sample preservation fluid or material 70, that may be contained in the interior space 20 may not be allowed to travel outside of the interior space 20, as shown in FIG. 3A. However, when the aperture 22 is open such that the annular blocking member 62 is not covering the aperture 22, the fluid or material 70 that may be contained in the interior space 20 may be allowed to travel outside of the interior space 20, such as into the reservoir 40 of the tube 14, as shown in FIG. 3B. The fluid or material 70 contained in the interior space may be beneficial for preserving sample 72, such as body fluids (i.e., saliva, urine, etc.) placed in the reservoir 40 of the tube 14, similarly as described above. Furthermore, any number of mechanisms may prevent the sample preserving fluid or material 72 from being released from the interior space 20 until the cap 12 is at least partially secured to the tube 14.

[0076] In the embodiment shown by way of example in FIGS 3A-3C, the annular blocking member 62 may be configured to interact with one or more features, such as a coupling member

50, of the tube 14 such that as the cap 12 is being securely coupled to the tube 14, the one or more features of either the tube 14 or annular blocking member 62 can cause the annular blocking member 62 to move from a position where the annular blocking member 62 is covering the aperture 22 to a position where the annular blocking member 62 is not covering the aperture 22, thus allowing the sample preserving fluid or material 72 to release from the interior space 20 and interact with the sample 72.

[0077] Figure 3C shows a cross section of the tube 14, having a containment wall 32 defining a reservoir 40 for sample collection. The tube 14 can include a coupling member 50 for engaging the coupling feature 48 of the annular blocking member 62.

[0078] An example method of use of a sample collection device 200 can include the sample collection device 200 supplied with sample preservation fluid 70 in the interior space 20 of the cap 12, and with the annular blocking member 62 covering the aperture 22 in order to prevent the passage of sample preservation fluid 70 through the aperture 22. In this embodiment, sample fluid 72, such as saliva or urine, can be placed in the reservoir 40 of the tube 14. The cap 12 may then be securely coupled, such as threadably engaged, onto the tube 14 causing the coupling features 48 of the annular blocking member 62 to engage the coupling member 50 of the tube 14. The annular blocking member 62 can then threadably engage the engagement features, such as threads, along the side of the inner walls. This can cause the annular blocking member 62 to move away from the aperture 22 so that it no longer covers the aperture 22. This, in turn, can release at least some of the sample preservation fluid 70 into the reservoir 40 of the tube 14, where it can mix with the sample fluid 72, thereby preserving it.

[0079] In some embodiments, the sample collection device 300, as shown by way of example in FIGS 4A and 4B, cap 12 includes at least one coupling feature or a wedge 90 which is shaped and configured to interact with a complimenting coupling feature or a flange 92 of the tube 14. In this embodiment, the wedge 90 and flange 92 are extending along an inside surface of the cap 12 and tube 14. For example, when the cap 12 is coupled to the tube 14, the wedge 90 can engage the flange 92 and form a secure engagement between the cap 12 and the tube 14. Furthermore, once the wedge 90 and flange 92 have been completely engaged with each other, such as the locked configuration 96 shown by way of example in FIG. 4B, the engagement between the wedge 90 and the flange 92 may not be releasable by at least the sample donor. Therefore, once the cap 12 becomes engaged to the tube 14 such that the wedge 90 and flange 92 are securely engaged with each other, the cap 12 may no longer be disengaged from the

tube 14 by at least the sample donor. This can prevent at least the sample donor from contaminating the sample body fluid that was deposited in the tube 14, as well as protect the sample donor from contact with the sample preservation solution. FIG. 4B shows sample embodiments of the unlocked configuration 94 and locked configuration 96 between the wedge 90 and flange 92.

[0080] In some embodiments, the sample collection device 400, as shown by way of example in FIGS. 5A and 5B, the wedge 90 and flange 92 are extending along an outside surface of the cap 12 and tube 14, respectively. Figure 5B shows sample embodiments of the unlocked configuration 94 and locked configuration 96 between the wedge 90 and flange 92.

[0081] In some embodiments, the sample collection device 500, as shown by way of example in FIG. 6, where the cap 12 includes one or more sealed cavities 110 containing a sealing substance 112, such as glue. Any one sealed cavity 110 may be either operatively associated or positioned adjacent engagement features 34, such as threads, on the cap 12 such that when the cap 12 is coupled to the tube 14 the one or more sealed cavities 110 may be broken by one or more features or end 150 of the tube 12. Once the sealed cavity 110 is broken, a sealing substance 112, such as glue, may be released from the sealed cavity 110 and cause the cap 12 to become permanently secured to the tube 14.

[0082] Any number of features may be included with the cap 12 or tube 14 which may assist in preventing unwanted decoupling of the cap 12 from the tube 14, such as to prevent contamination. Additionally or alternatively, either the cap 12 or tube 14 may include a “tamper evident” feature 160 which may become altered such that it can be known to a user or sample collector if the cap 12 has been unfavorably decoupled from the tube 14. As shown by way of example in FIGS. 7A and 7B, the cap 12 may include a tamper evident feature 160 which may be comprised of a ring that is releasably attached to the open end 162 of the cap 12 such that when the cap 12 is unfavorably decoupled from the tube 14, the tamper evident feature 160 can permanently release its attachment from the cap 12, as shown in FIG. 7B. Once the tamper evident feature 160 is permanently detached from the cap 12, any observer of the cap 12 can determine that the cap 12 had been unfavorably decoupled from the tube 12, thus providing a warning of sample contamination, for example.

[0083] Those skilled in the art will recognize that numerous equivalent embodiments can be used to obtain the benefits provided by the sample collection devices disclosed herein. For example, while this specification refers to certain elements being in the cap 12, and others in

the tube 14, one skilled in the art would recognize that reversing the elements in the cap 12 to be in the tube 14 and vice-versa, would be an equivalent.

[0084] In some embodiments, a solution for preserving cells in one or more bodily fluids, such as saliva and urine, is disclosed. The solution for preserving cells may be beneficial for further separation into cell types and downstream molecular analysis that allows for storage of cells in the body fluid to retain their antigenicity and cellular architecture. The solution may contain at least one chemical fixing agent, such as but not limited to paraformaldehyde, and at least one protease inhibitor. In some embodiments, the solution may further contain one or more of at least one antimicrobial agent, and serum proteins from human and/or other animal species. The solution can be buffered at a pH from between about 6.4 to about 8.4, preferably from between about 7.2 to about 7.6.

[0085] For purposes of the disclosure, “preserving cells” means preventing the cells from having their antigens degraded, such that they can be purified or enriched based on their antigens, and preventing alterations in the cellular epigenome. The “epigenome” means the state or pattern of alteration of genomic DNA by covalent modification of the DNA or of proteins bound to the DNA. Examples of such alteration include methylation at the 5 position of cytosine in a CpG dinucleotide, acetylation of lysine residues of histones, and other heritable or non-heritable changes that do not result from changes in the underlying DNA sequence.

[0086] In some embodiments, concentrations of agents in the following description can be those of the sample preserving solution itself. Depending upon the bodily fluid, and in the case of saliva, about an equal volume of solution and body fluid can be mixed together. This preferably results in the cells from the body fluids retaining their antigenicity and DNA integrity for at least one week at room temperature.

[0087] In some embodiments of the disclosure, the volume of preservation solution held within the device and deployed may be between about 100 and about 500 ml, which is relevant, for example, for the preservation of cells in urine. As such, the preservation solution for urine may be anywhere between about ten times (10x) concentrated solution to a one-point five time (1.5x) solution for urine.

[0088] A “chemical fixing agent”, according to some embodiments, is a chemical cross-linking compound used to alter cell components such that the cells resist degradation. The chemical fixing agents can also serve to cross-link histones and other DNA-binding proteins to the DNA. Such agents may be known in the art and include, without limitation, paraformaldehyde,

formaldehyde, formalin, aldehydes, alcohol, oxidizing agents, Mercurials, Picrates, Hepes-glutamic acid buffer-mediated organic solvent protection effect (HOPE), fixative combinations such as Zambonis fixative, combinations of aldehydes, and synthetic cross-linking reagents. In some embodiments, the chemical fixing agent is paraformaldehyde. In some embodiments, the chemical fixing agent is present at a concentration of about 1% (v/v).

[0089] To protect the cells from degradation by proteases present in the body fluids, in some embodiments, the solution can contain at least one protease inhibitor. In some embodiments, the protease inhibitor can be selected from the group consisting of Aspartic protease inhibitors, Cysteine protease inhibitors, Metalloprotease inhibitors, Serine protease inhibitors (e.g., serpins), Threonine protease inhibitors, Trypsin inhibitors, and Kunitz STI protease inhibitor. Some specific, non-limiting, examples include sodium azide, PMSF, Aprotinin, leupeptin, pepstatin, natural or synthetic proteinase inhibitors, and cocktail mixtures of protease inhibitors. Suitable concentrations of these inhibitors can include, without limitation, PMSF (Phenylmethylsulfonyl fluoride) Serine proteases at about 0.1-1 mM, Benzamidine Serine proteases at about 1 mM, Pepstatin A Acid proteases at about 1 µg/ml, Leupeptin Thiol proteases at about 1 µg/ml, Aprotinin Serine proteases at about 5 µg/ml, and Antipain Thiol proteases at about 1 µg/ml. In certain embodiments, the protease inhibitor is sodium azide at a concentration of about 0.01% (w/v).

[0090] To prevent damage to the cells from microbial contamination, some embodiments of the solution contain at least one antimicrobial agent. Suitable antimicrobial agents include, without limitation, antibacterial and antifungal antibiotics.

[0091] Preservation of cell architecture is enhanced by the presence of serum proteins, which may optionally be added to the solution in some embodiments. Additionally serum proteins may be used to neutralize osmotic difference between cells and solution. These can be from human or other animal sources. In some cases, whole serum may be used. For example, fetal bovine serum may be added, in some embodiments at about 1% (v/v).

[0092] The solution according to the disclosure may include any combination of the foregoing embodiments.

[0093] In some embodiments of the disclosure, a method for preserving cells in one or more bodily fluids is disclosed. The method for preserving the cells can comprise contacting the body fluids with the solution according to the present disclosure. The body fluids can contain a variety of cell types and the cells in the body fluids can be preserved by the solution according

to the present disclosure. While not critical to the present disclosure, a ratio of solution to body fluids of from about 1 to 1 is typically used.

[0094] The following examples are intended to further illustrate some embodiments of the solutions and methods for preserving cells in body fluids and are not to be construed to limit the scope of this disclosure.

[0095] For example, a solution of PBS pH 7.4, 1% Paraformaldehyde, 1% FBS, and 0.01% NaN₃ can be added at a 1:1 ration with saliva, then T-cells can be purified and DNA extracted. The results of such a process are shown in FIG. 8. These results can demonstrate that the integrity of the antigenicity and DNA of T-cells was maintained for at least one week.

[0096] In some embodiments of the present disclosure, a method is disclosed which provides a sample of one or more body fluids, such as saliva or urine, comprising chemically fixed cells, and optionally centrifuging the body fluid sample to separate DNA and other soluble material from a pellet of cells including bacteria and debris. The method can further include enriching white blood cells, including lymphocyte cells, from other contents of the pellet. Additionally, specific cells may be isolated using antibodies conjugated to magnetic beads targeted to cell specific markers.

[0097] In some embodiments, the disclosure provides a method for isolating a particular type of white blood cell, specifically including, but not limited to lymphocytes, from bodily fluids (i.e., saliva, urine, etc.), comprising, for example one or more (and in some embodiments, several or all of the steps): providing a body fluid sample comprising chemically fixed cells, optionally centrifuging the body fluid sample to obtain a pellet comprising cells, optionally resuspending the pellet in buffer, subjecting the re-suspended pellet to density gradient separation to obtain a layer of a mixture of white blood cell types (including lymphocytes), contacting the mixture of cell types with a solution containing specific binding agents for an epitope found on a particular type of white blood cell, and separating the particular type of white blood cell (including lymphocytes) from the mixture of white blood cell types.

[0098] In some embodiments, the specific binding agents can include magnetic beads coupled to antibodies specific to an epitope found on a particular type of white blood cell, and separating may comprise magnetically separating the particular type of white blood cell (including lymphocytes) from the mixture of white blood cell types, though any method (and corresponding system/device) for separating cell types from one another is within the scope of this disclosure. Magnetic separation is but one method for doing so.

[0099] The cells can be chemically fixed prior to being subjected to the method according to this disclosure. The cells can be chemically fixed by, e.g., contacting a sample of saliva with a chemical fixation solution. This is done to preserve the cells over time at ambient temperatures. This can also allow for a complete study of the epigenome as it allows histone modifications and other protein-DNA interactions to be studied from the deposited body fluid samples. Histones must be chemically fixed to the DNA in order to be studied. Without fixation, the histones generally cannot remain bound to the DNA and the proteins can degrade over time.

[00100] In some embodiments, the buffer can comprise sodium azide, the buffer can comprise phosphate buffered saline and sodium azide, In some embodiments, the buffer may further comprise fetal bovine serum. In some embodiments, the buffer is at a pH from between about 7.2 to about 7.6.

[00101] In some embodiments, the cells are washed once in buffer. This in practice removes soluble material and in the case of saliva it removes what has been classified as the “buccal” layer (Dos-Santos *et al.*, 2009).

[00102] In some embodiments, the mixture of white blood cells is washed one or more times in buffer prior to separating. This is preferably done to remove any remaining density gradient solution from the mixture of cell types.

[00103] In the process, the antibodies may bind to the particular type of white blood cells, thus binding the particular type of white blood cells to the magnetic beads. The particular type of white blood cells can then be separated from any other cell types by placing the magnetic beads in a magnetic field and removing any remaining liquid to obtain isolated cells of the particular type of white blood cells.

[00104] In some embodiments, the particular type of white blood cells can be a lymphocyte, where the lymphocyte may be a T-cell. In such embodiments, the antibodies used may be specific to an antigen specific to T-cells (e.g., the antigen being CD4). In some embodiments, the isolated blood cells may then be frozen prior to further processing, such as prior to epigenetic analysis.

[00105] The following example is intended to further illustrate an example method embodiment of the present disclosure and is not intended to limit the scope of the disclosure.

[00106] Example: Isolating T-cells from a bodily fluid (e.g., saliva)

[00107] Saliva is collected, and the saliva is mixed with preservation solution. The cells are then pelleted by centrifugation and the processing solution is removed. The cells are then re-suspended in about 6 ml buffer (PBS, pH 7.4), 1% FBS, .01 % NaN₃, then washed once in a buffer and repelleted. The pellet are resuspended in about 6 mL PBS-15 FBS-.01%NaN₃ and subjected to density gradient centrifugation using 1.082 -1.072 g/ml of Ficoll[®] (GE Healthcare). The white-blood cells are spun to the interface of the polysaccharides and buffer while the bacteria, debris, and any other particulate matter were pelleted at the bottom of the tube. The cells are extracted from the tube and placed in a new tube. The cells are then washed in Hank's Balanced Salt Solution once and then washed with the PBS-NaN₃-FBS buffer once to remove remaining density gradient solution that may have been taken while extracting the white blood cells from the interface.

[00108] The sample now includes highly enriched white-blood cells with minimal bacteria and minimal debris. This step can also greatly decrease other cell types, such as epithelial cells. The cells can then be incubated in buffer (PBS-NaN₃-FBS) with antibody targeted against CD4 conjugated to magnetic beads (Dynabeads[®] Invitrogen[®]). The samples can then be placed in a magnetic field, the beads brought to the side of the tube, and the liquid removed. The liquid may contain everything not bound to the beads through the antibody. The T-cells can be bound to the antibody and not removed due to the magnetic field. The beads and the attached cells can be washed in buffer to eliminate any non-specific or weak binding of other cells, bacteria, or other debris found in bodily fluids, such as saliva or urine. The cells can then be frozen for later downstream processing and analysis. The isolation of T-cells can be confirmed by light microscopy (T-cells are very distinct compared to epithelial cells and bacteria) (see FIG. 9). Additionally, flow cytometry and F.A.C.S. analysis using antibodies against CD3, CD4, and CD8 can confirm visual assessment of the isolated cells. The T-cells may then be tittered from the body fluid to determine the number of T-cells per unit of body fluid (ml) in order to determine the amount of body fluid, such as saliva or urine, for an adequate number of cells for downstream experimentation (see FIG. 9 and 10). The isolated cells can be shown to have DNA devoid of degradation and appropriate for downstream use (see FIG. 8).

[00109] Any and all references to publications or other documents, including but not limited to, patents, patent applications, articles, webpages, books, etc., presented in the present application, are herein incorporated by reference in their entirety.

[00110] Although a few variations have been described in detail above, other

modifications are possible. For example, any logic flow depicted in the accompanying figures and described herein does not require the particular order shown, or sequential order, to achieve desirable results. Other implementations may be within the scope of at least some of the following exemplary claims.

[00111] Example embodiments of the devices, systems and methods have been described herein. As noted elsewhere, these embodiments have been described for illustrative purposes only and are not limiting. Other embodiments are possible and are covered by the disclosure, which will be apparent from the teachings contained herein. Thus, the breadth and scope of the disclosure should not be limited by any of the above-described embodiments but should be defined only in accordance with claims supported by the present disclosure and their equivalents. Moreover, embodiments of the subject disclosure may include methods, systems and devices which may further include any and all elements from any other disclosed methods, systems, and devices, including any and all elements corresponding to collection, preservation, separating and isolating of cells from bodily fluids (e.g., saliva, urine), as well as the collection of other substances, including toxic and/or hazardous substances/fluids (as well as the preservation, separating and isolation of components thereof). In other words, elements from one or another disclosed embodiments may be interchangeable with elements from other disclosed embodiments.

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What is claimed is:

1. A biological sample collection system, the system comprising:
 - a sample collection vessel comprising
 - a sample collection reservoir,
 - a connection member, and
 - an aperture for receiving a biological sample;
 - a cap comprising
 - an aperture,
 - a reagent chamber storing a reagent therein, and
 - a connection member complementary to the connection member of the sample collection vessel; and
 - a moveable annular valve in the aperture of the cap, the movable annular valve comprising
 - a vent,
 - a first cylinder comprising an aperture,
 - a second cylinder comprising the vent, the second cylinder positioned in the aperture of the first cylinder,
 - a closed configuration, and
 - an open configuration, wherein
 - in the annular valve's closed configuration, the first and second cylinders create a fluid-tight seal with the cap and the first cylinder obstructs the vent to retain the reagent in the reagent chamber,
 - the first cylinder and second cylinder are relatively moveable to thereby change the annular valve from the closed configuration to the open configuration, and

in the annular valve's open configuration, the first cylinder does not obstruct the vent to thereby allow flow of the reagent from the reagent chamber, through the vent, and into the sample collection reservoir.

2. The biological sample collection system of claim 1, wherein the second cylinder comprises a sidewall and the sidewall comprises the vent, wherein the annular valve's closed configuration comprises a sidewall of the first cylinder obstructing the vent and the annular valve's open configuration comprises the sidewall of the first cylinder not obstructing the vent.

3. The biological sample collection system of claim 1, wherein the first and second cylinder's relative movement, from the annular valve's closed configuration to the open configuration, is translational along a longitudinal axis of the cap.

4. The biological sample collection system of claim 1, wherein the first and second cylinder's relative movement, from the annular valve's closed configuration to the open configuration, comprises the second cylinder moving in the aperture of the first cylinder.

5. The biological sample collection system of claim 1, wherein the first cylinder comprises a press-fit connection with the cap.

6. The biological sample collection system of claim 1, wherein the second cylinder comprises a plurality of vents and the first cylinder obstructs the plurality of vents in the annular valve's closed configuration.

7. The biological sample collection system of claim 1, wherein the annular valve comprises a flange and the annular valve with flange comprises a width larger than a width of the collection vessel's aperture.

8. The biological sample collection system of claim 7, wherein interaction between the flange and a wall of the sample collection vessel causes the first and second cylinders to move relatively and change the annular valve from the closed configuration to the open configuration.

9. The biological sample collection system of claim 1, further comprising a funnel attachable to the sample collection vessel

10. The biological sample collection system of claim 1, wherein the vent is at least partially unobstructed in the annular valve's open configuration.

11. The biological sample collection system of claim 1, wherein the vent is fully unobstructed in the annular valve's open configuration.

12. The biological sample collection system of claim 1, wherein the first and second cylinders comprise generally constant exterior diameters.

13. The biological sample collection system of claim 12, wherein the annular valve comprises a flange extending from at least one of the first and second cylinders.

14. The biological sample collection system of claim 1, wherein the connection members comprise a threaded connection.

15. The biological sample collection system of claim 1, wherein the annular valve comprises a sliding connection between the first and second cylinders.

16. The biological sample collection system of claim 1, wherein the sample collection system comprises a separable two-piece sample collection system, the sample collection vessel comprising a first piece of the separable two-piece sample collection system, and the cap with movable annular valve comprising a second piece of the separable two-piece sample collection system.

17. The biological sample collection system of claim 1, wherein the first cylinder comprises threads on an interior sidewall configured to mate with threads on an exterior sidewall of the second cylinder.

18. The biological sample collection system of claim 1, wherein a diameter of an inner wall of the first cylinder is sufficiently equal to a diameter of an outer wall of the second cylinder to create a fluid-tight connection therebetween and allow relative movement.

19. The biological sample collection system of claim 1, wherein the system is configured such that connecting the cap to the sample collection vessel causes the annular valve to move from the closed configuration to the open configuration.

20. The biological sample collection system of claim 1, wherein

the system is configured such that connecting the cap to the sample collection vessel causes the annular valve to move from the closed configuration to the open configuration, wherein

the second cylinder comprises a sidewall and the sidewall comprises the vent, wherein

the annular valve's closed configuration comprises a sidewall of the first cylinder obstructing the vent and the annular valve's open configuration comprises the sidewall of the first cylinder not obstructing the vent, and wherein

the first and second cylinder's relative movement, from the annular valve's closed configuration to the open configuration, is translational along a longitudinal axis of the cap.

ABSTRACT

The disclosure relates to devices, solutions and methods for collecting and processing samples of bodily fluids containing cells (as well as embodiments for the collection, and processing and/or analysis of other fluids including toxic and/or hazardous substances/fluids). In addition, the disclosure relates generally to function genomic studies and to the isolation and preservation of cells from saliva and other bodily fluids (e.g., urine), for cellular analysis. With respect to devices for collection of bodily fluids, some embodiments include two mating bodies, a cap and a tube (for example), where, in some embodiments, the cap includes a closed interior space for holding a sample preservative solution and mates with the tube to constitute the (closed) sample collection device. Upon mating, the preservation solution flows into the closed interior space to preserve cells in the bodily fluid. The tube is configured to receive a donor sample of bodily fluid (e.g., saliva, urine), which can then be subjected to processing to extract a plurality of cells. The plurality of cells can be further processed to isolate one and/or another cell type therefrom. The plurality of cells, as well as the isolated cell type(s), can be analyzed for functional genomic and epigenetic studies, as well as biomarker discovery.

1/9

FIG. 1

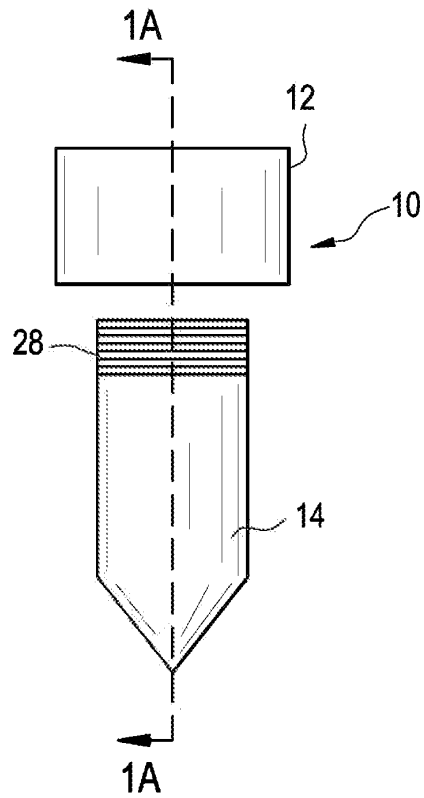


FIG. 1A

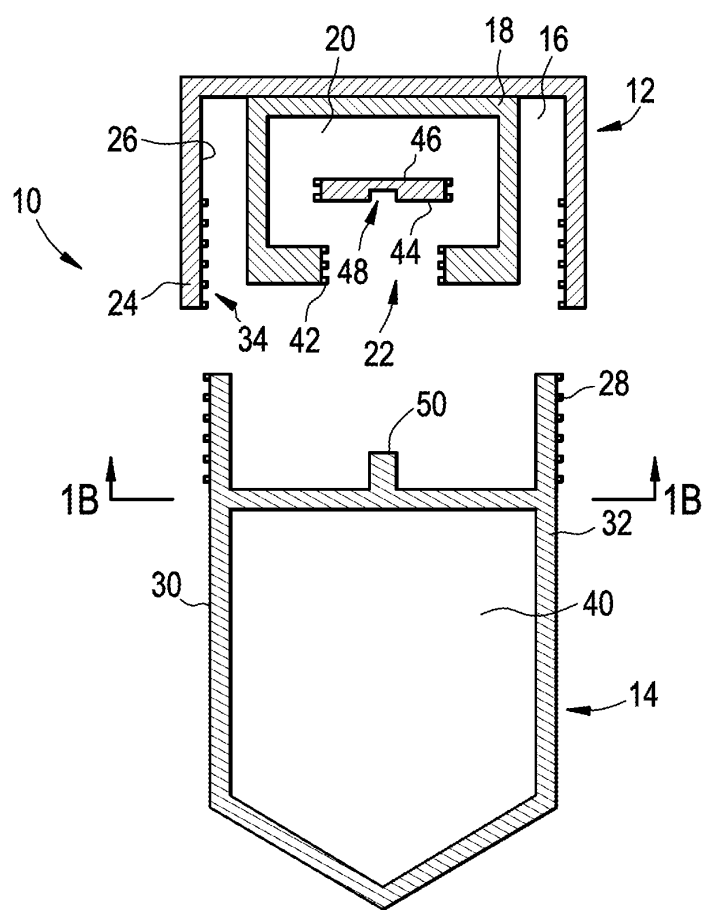


FIG. 1B

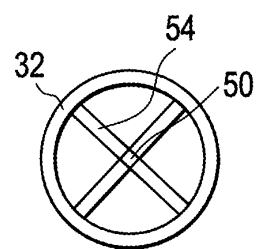


FIG. 2A

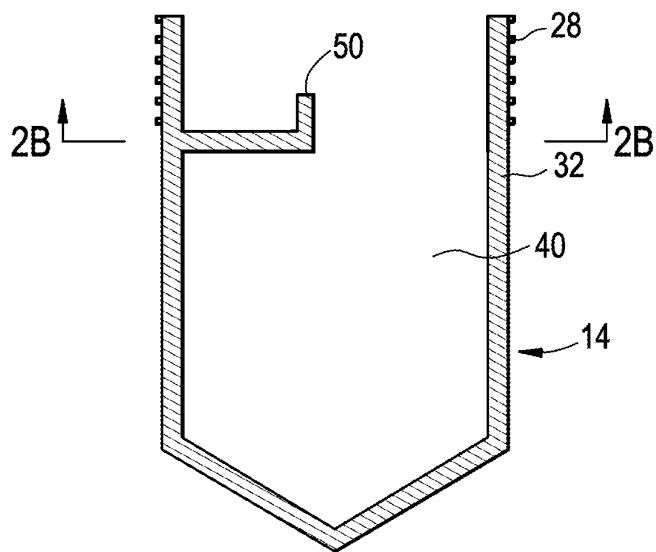
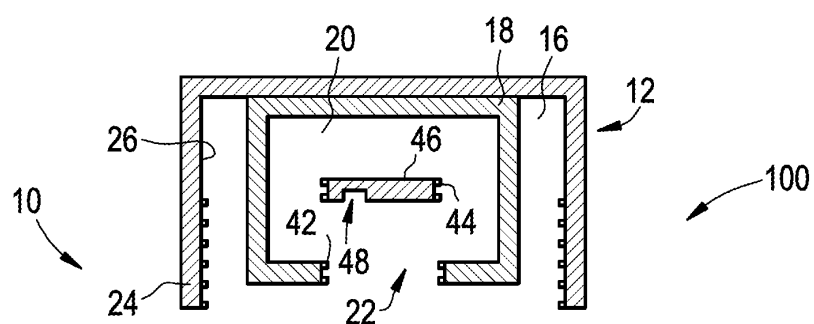


FIG. 2B

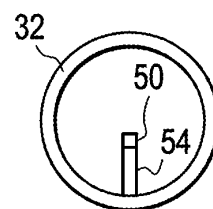


FIG. 3A

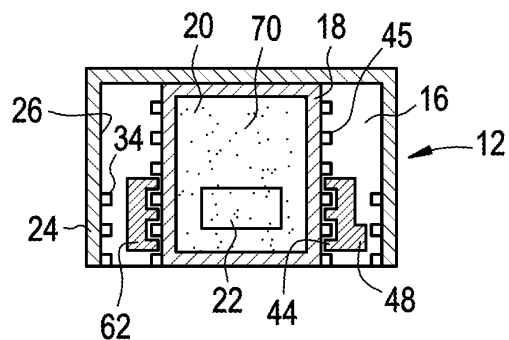


FIG. 3B

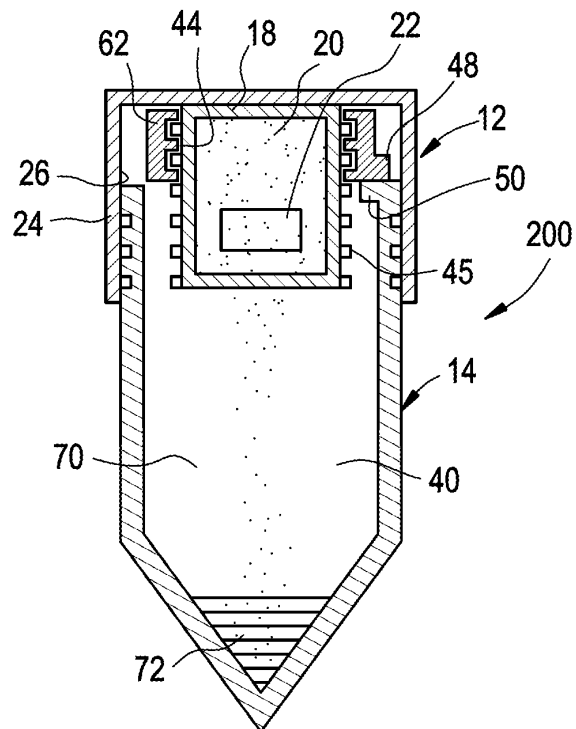


FIG. 3C

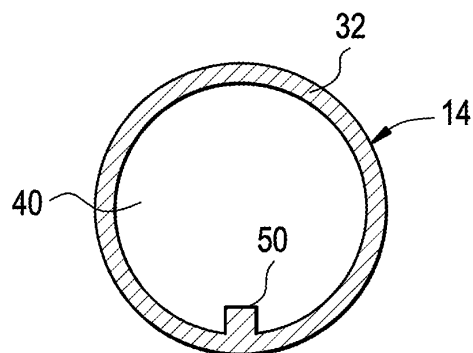


FIG. 4A

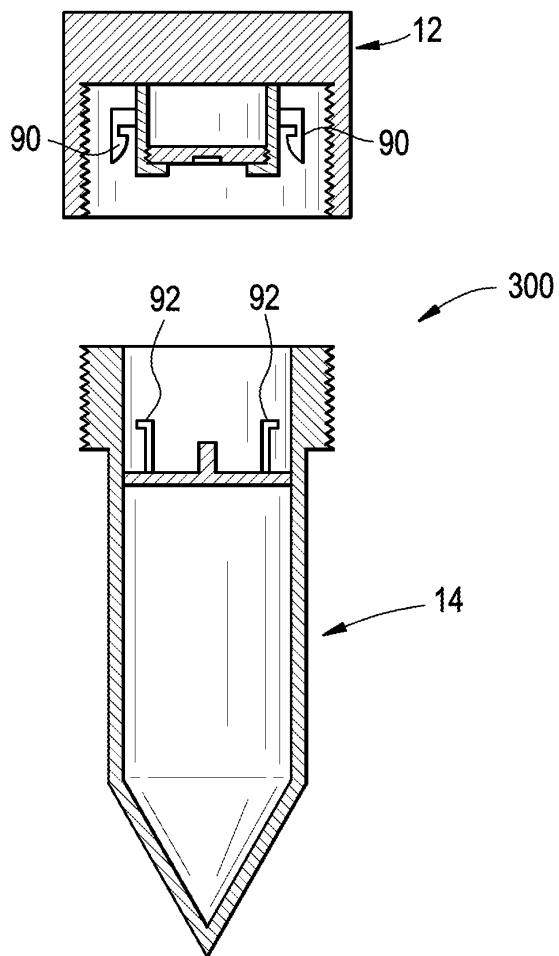


FIG. 4B

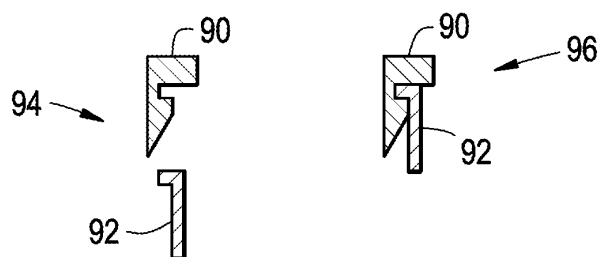


FIG. 5A

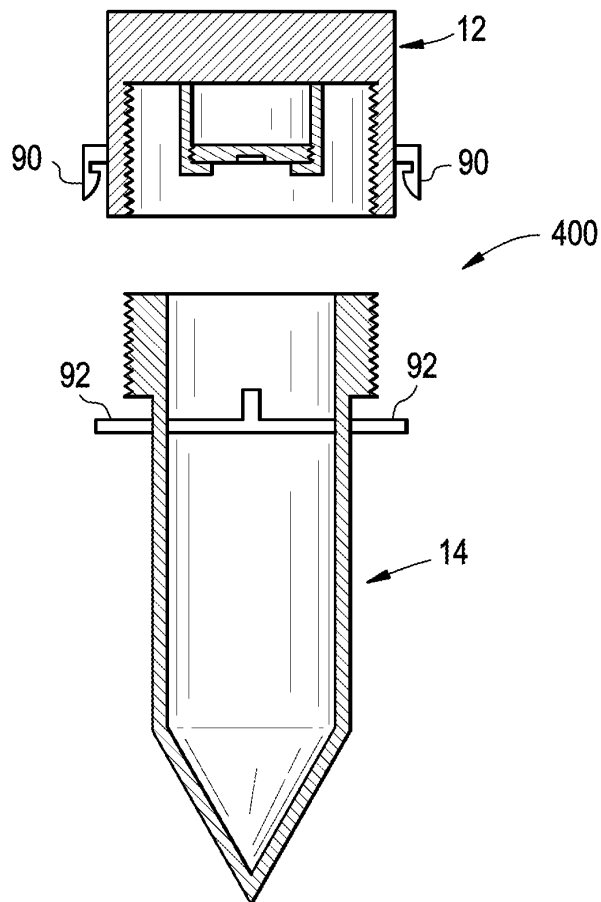


FIG. 5B

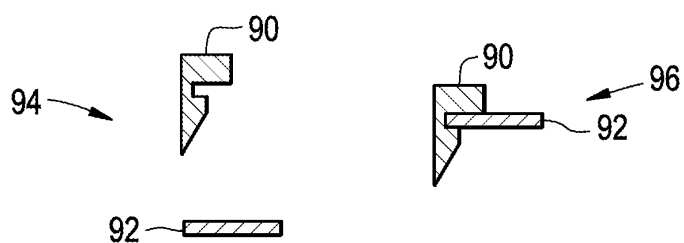


FIG. 6

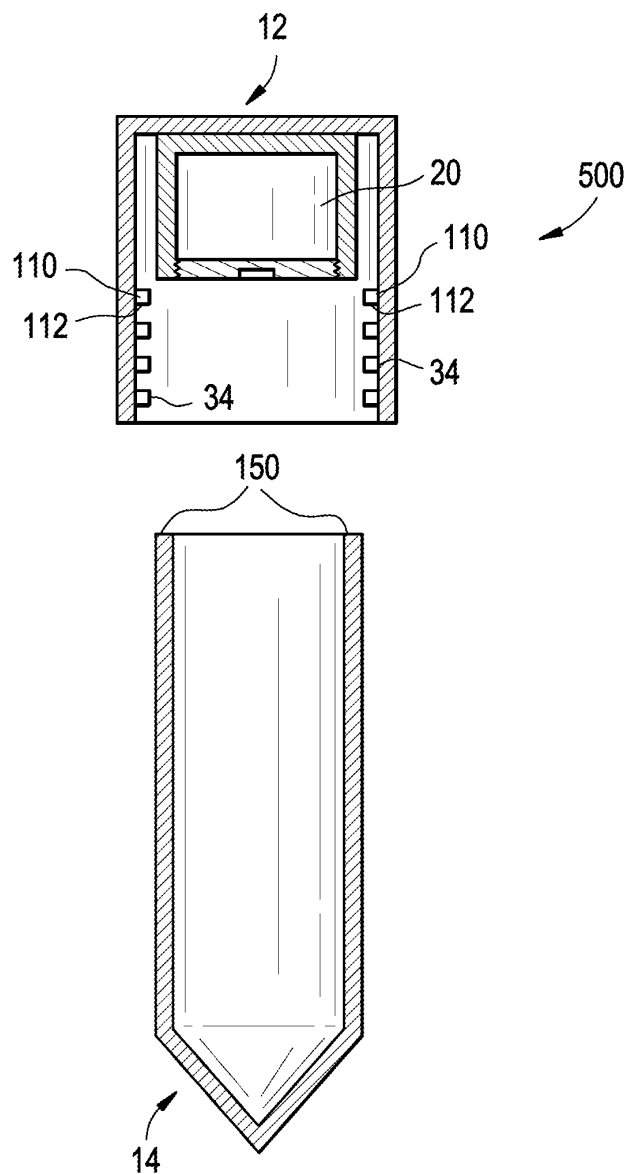


FIG. 7A

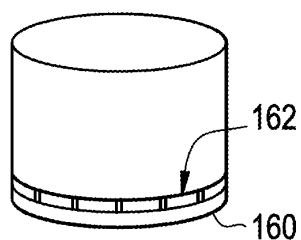


FIG. 7B

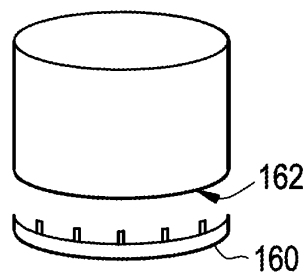
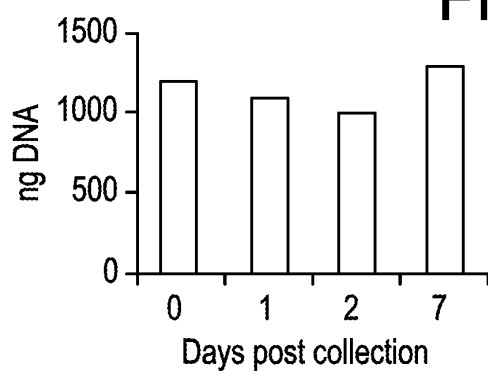


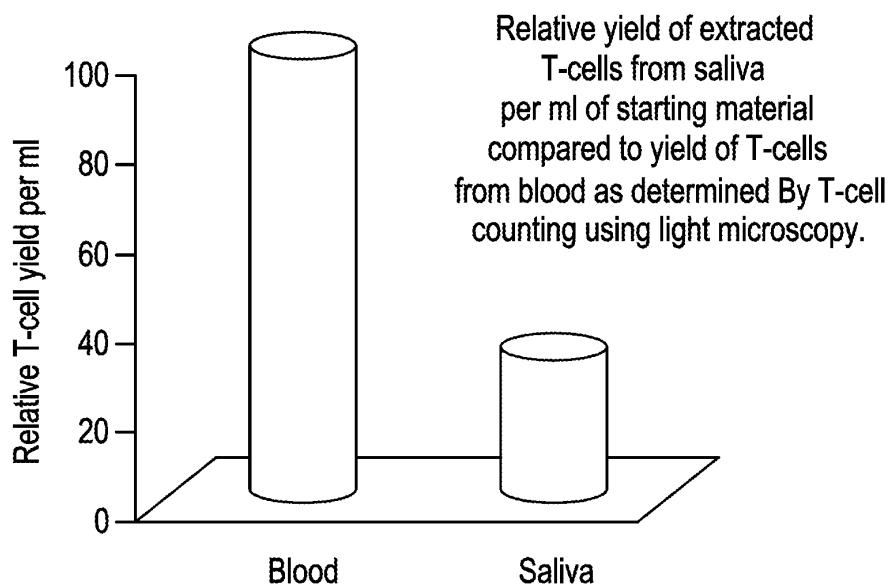
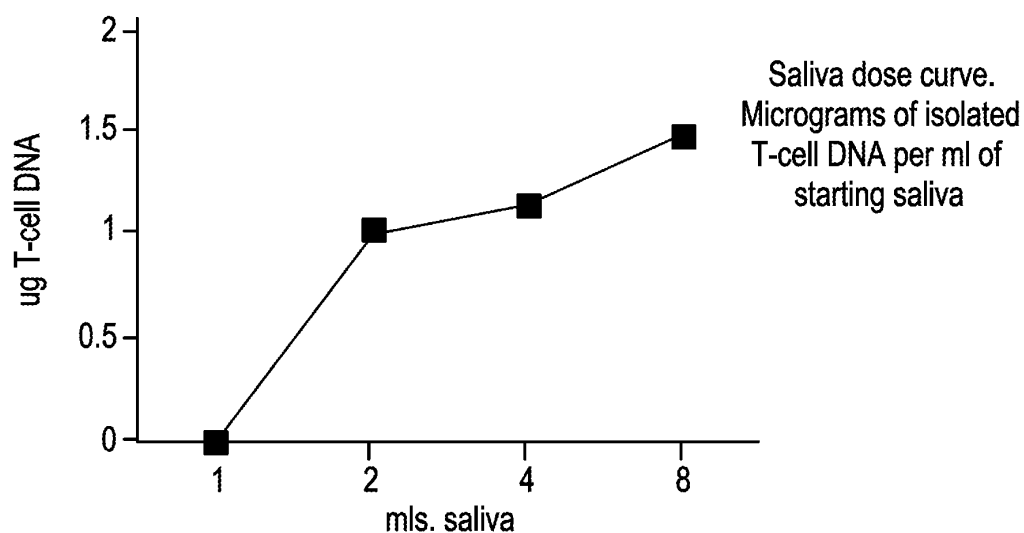
FIG. 8



Time course of DNA yield of isolated T-cells after saliva samples stored in preservation solution at room temperature and then proceed.



DNA extracted from isolated T-cells after stored in preservation solution for indicated time.

FIG. 9**FIG. 10**

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	DEVICE FOR SAMPLE COLLECTION
--------------------	------------------------------

As the below named inventor, I hereby declare that:

This declaration is directed to: ☐ The attached application, or ☒ United States application or PCT international application number 15/227,693 filed on August 3, 2016

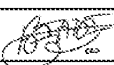
The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

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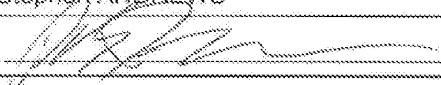
LEGAL NAME OF INVENTOR	
Inventor: <u>Youssef BIADILLAH</u>	Date (Optional): _____
Signature: <u></u>	

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	DEVICE FOR SAMPLE COLLECTION
As the below named inventor, I hereby declare that: This declaration is directed to: ☐ The attached application, or ☒ United States application or PCT international application number <u>15/227,693</u> filed on <u>August 3, 2016</u> The above identified application was made or authorized to be made by me. I believe that I am the original inventor or an original joint inventor of a claimed invention in the application. I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both. WARNING: Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.	
LEGAL NAME OF INVENTOR	
Inventor: <u>Stephen ANDREWS</u>	Date (Optional): <u>Aug 3, 2016</u>
Signature: 	
Note: An application data sheet (PTO/SF/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.	

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-4144 and select option 2.

CERTIFICATION AND REQUEST FOR PRIORITIZED EXAMINATION UNDER 37 CFR 1.102(e) (Page 1 of 1)			
First Named Inventor:	Youssef BIADILLAH	Nonprovisional Application Number (if known):	Not Yet Assigned
Title of Invention:	BIOLOGICAL COLLECTION SYSTEM		
APPLICANT HEREBY CERTIFIES THE FOLLOWING AND REQUESTS PRIORITIZED EXAMINATION FOR THE ABOVE-IDENTIFIED APPLICATION. 1. The processing fee set forth in 37 CFR 1.17(i)(1) and the prioritized examination fee set forth in 37 CFR 1.17(c) have been filed with the request. The publication fee requirement is met because that fee, set forth in 37 CFR 1.18(d), is currently \$0. The basic filing fee, search fee, and examination fee are filed with the request or have been already been paid. I understand that any required excess claims fees or application size fee must be paid for the application. 2. I understand that the application may not contain, or be amended to contain, more than four independent claims, more than thirty total claims, or any multiple dependent claims, and that any request for an extension of time will cause an outstanding Track I request to be dismissed. 3. The applicable box is checked below: I. ☒ Original Application (Track One) - Prioritized Examination under § 1.102(e)(1) i. (a) The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a). This certification and request is being filed with the utility application via EFS-Web. ---OR--- (b) The application is an original nonprovisional plant application filed under 35 U.S.C. 111(a). This certification and request is being filed with the plant application in paper. ii. An executed inventor's oath or declaration under 37 CFR 1.63 or 37 CFR 1.64 for each inventor, <u>or</u> the application data sheet meeting the conditions specified in 37 CFR 1.53(f)(3)(i) is filed with the application. II. ☐ Request for Continued Examination - Prioritized Examination under § 1.102(e)(2) i. A request for continued examination has been filed with, or prior to, this form. ii. If the application is a utility application, this certification and request is being filed via EFS-Web. iii. The application is an original nonprovisional utility application filed under 35 U.S.C. 111(a), or is a national stage entry under 35 U.S.C. 371. iv. This certification and request is being filed prior to the mailing of a first Office action responsive to the request for continued examination. v. No prior request for continued examination has been granted prioritized examination status under 37 CFR 1.102(e)(2).			
Signature /Chun L. Yu/		Date October 25, 2021	
Name (Print/Typed) Chun L. Yu, Ph.D.		Practitioner Registration Number 68,138	
Note: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. Submit multiple forms if more than one signature is required.*			
☐ *Total of <u>1</u> forms are submitted.			
I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with 37 C.F.R. § 1.6(a)(4). Dated: October 25, 2021 Electronic Signature for Chun L. Yu, Ph.D.: /Chun L. Yu/			



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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
17/510,003	10/25/2021	Youssef BIADILLAH	OSHH-001/C05US

CONFIRMATION NO. 3950

FORMALITIES LETTER



58249
COOLEY LLP
ATTN: IP Docketing Department
1299 Pennsylvania Avenue, NW
Suite 700
Washington, DC 20004

Date Mailed: 11/04/2021

NOTICE TO FILE CORRECTED APPLICATION PAPERS

Filing Date Granted

An application number and filing date have been accorded to this application. The application is informal since it does not comply with the regulations for the reason(s) indicated below. Applicant is given **TWO MONTHS** from the date of this Notice within which to correct the informalities indicated below. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

The required item(s) identified below must be timely submitted to avoid abandonment:

- Replacement drawings in compliance with 37 CFR 1.84 and 37 CFR 1.121(d) are required. The drawings submitted are not acceptable because:
 - The drawings contain excessive text. Suitable descriptive legends may be used, or may be required by the Examiner where necessary for understanding of the drawing but should contain as few words as possible (see 37 CFR 1.84(o)). See Figure(s) 8, 9, 10.

Applicant is cautioned that correction of the above items may cause the specification and drawings page count to exceed 100 pages. If the specification and drawings exceed 100 pages, applicant will need to submit the required application size fee.

Replies must be received in the USPTO within the set time period or must include a proper Certificate of Mailing or Transmission under 37 CFR 1.8 with a mailing or transmission date within the set time period. For more information and a suggested format, see Form PTO/SB/92 and MPEP 512.

Replies should be mailed to:

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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO.	TOT CLAIMS	IND CLAIMS
17/510,003	10/25/2021		1820	OSHH-001/C05US	20	1

CONFIRMATION NO. 3950

FILING RECEIPT



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Date Mailed: 11/04/2021

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

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Inventor(s)

Youssef BIADILLAH, Geneva, SWITZERLAND;
Stephen D. ANDREWS, Falmouth, ME;

Applicant(s)

DNA GENOTEK, INC., Ottawa, CANADA;

Assignment For Published Patent Application

DNA GENOTEK, INC., Ottawa, CANADA

Power of Attorney: None

Domestic Priority data as claimed by applicant

This application is a CON of 16/023,772 06/29/2018
which is a CON of 15/227,693 08/03/2016 ABN
which is a CON of 14/127,832 12/19/2013 PAT 9442046
which is a 371 of PCT/US2012/043176 06/19/2012
which claims benefit of 61/598,601 02/14/2012
and claims benefit of 61/598,618 02/14/2012
and claims benefit of 61/498,584 06/19/2011

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see <http://www.uspto.gov> for more information.) - None.

Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: Yes

Permission to Access Search Results: Yes

Applicant may provide or rescind an authorization for access using Form PTO/SB/39 or Form PTO/SB/69 as appropriate.

If Required, Foreign Filing License Granted: 11/03/2021

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 17/510,003**

Projected Publication Date: To Be Determined - pending completion of Corrected Papers

Non-Publication Request: No

Early Publication Request: Yes

Title

BIOLOGICAL COLLECTION SYSTEM

Preliminary Class

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

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Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

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page 2 of 4

this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific countries such as China, Korea and Mexico. For questions regarding patent enforcement issues, applicants may call the U.S. Government hotline at 1-866-999-HALT (1-866-999-4258).

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Title 37, Code of Federal Regulations, 5.11 & 5.15

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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
17/510,003	10/25/2021	Youssef BIADILLAH	OSHH-001/C05US

CONFIRMATION NO. 3950

FORMALITIES LETTER



58249
COOLEY LLP
ATTN: IP Docketing Department
1299 Pennsylvania Avenue, NW
Suite 700
Washington, DC 20004

Date Mailed: 11/04/2021

NOTICE TO FILE CORRECTED APPLICATION PAPERS

Filing Date Granted

An application number and filing date have been accorded to this application. The application is informal since it does not comply with the regulations for the reason(s) indicated below. Applicant is given **TWO MONTHS** from the date of this Notice within which to correct the informalities indicated below. Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

The required item(s) identified below must be timely submitted to avoid abandonment:

- Replacement drawings in compliance with 37 CFR 1.84 and 37 CFR 1.121(d) are required. The drawings submitted are not acceptable because:
 - The drawings contain excessive text. Suitable descriptive legends may be used, or may be required by the Examiner where necessary for understanding of the drawing but should contain as few words as possible (see 37 CFR 1.84(o)). See Figure(s) 8, 9, 10.

Applicant is cautioned that correction of the above items may cause the specification and drawings page count to exceed 100 pages. If the specification and drawings exceed 100 pages, applicant will need to submit the required application size fee.

Replies must be received in the USPTO within the set time period or must include a proper Certificate of Mailing or Transmission under 37 CFR 1.8 with a mailing or transmission date within the set time period. For more information and a suggested format, see Form PTO/SB/92 and MPEP 512.

Replies should be mailed to:

Mail Stop Missing Parts
Commissioner for Patents
P.O. Box 1450
Alexandria VA 22313-1450

Registered users of EFS-Web may alternatively submit their reply to this notice via EFS-Web, including a copy of this Notice and selecting the document description "Applicant response to Pre-Exam Formalities Notice".
<https://sportal.uspto.gov/authenticate/AuthenticateUserLocalEPF.html>

For more information about EFS-Web please call the USPTO Electronic Business Center at 1-866-217-9197 or visit our website at <http://www.uspto.gov/ebc>.

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Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at
(571) 272-4000 or (571) 272-4200 or 1-888-786-0101.

/cma/

Docket No.: OSHH-001/C05US 158166-2025
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor: Youssef BIADILLAH Confirmation No.: 3950
Application No.: 17/510,003 Group Art Unit: TBD
Filed: October 25, 2021 Examiner: TBD
For: BIOLOGICAL COLLECTION SYSTEM

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

STATEMENT IN SUPPORT OF SUBSTITUTE SPECIFICATION

Pursuant to 37 C.F.R. 1.121(b)(3) and 1.125, I hereby state that the content of the Substitute Specification submitted herewith and that of the specification filed on October 25, 2021, are the same. The Substitute Specification (marked-up and clean versions) is submitted to include the excessive text in FIGS. 8 and 9, which is deleted in the replacement sheets submitted herewith. Accordingly, no new matter is added.

Dated: January 4, 2022

Respectfully submitted,
COOLEY LLP

USPTO CUSTOMER NO. 58249

COOLEY LLP
ATTN: IP Docketing Department
1299 Pennsylvania Avenue NW, Suite 700
Washington, DC 20004

By: /Chun L. Yu/
(Chris) Chun L. Yu
Reg. No. 68,138

Tel: (212) 479-6463
Fax: (212) 479-6275

FIG. 7A

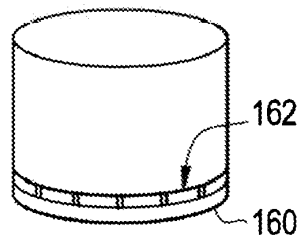


FIG. 7B

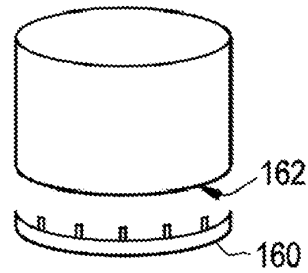


FIG. 8

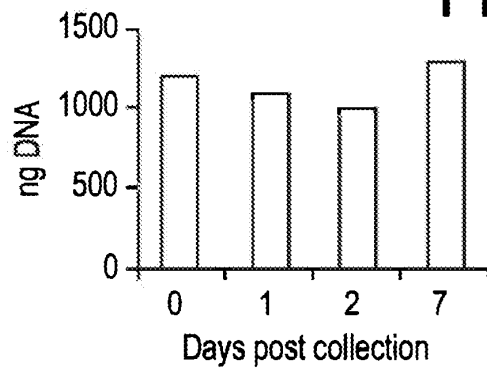


FIG. 9

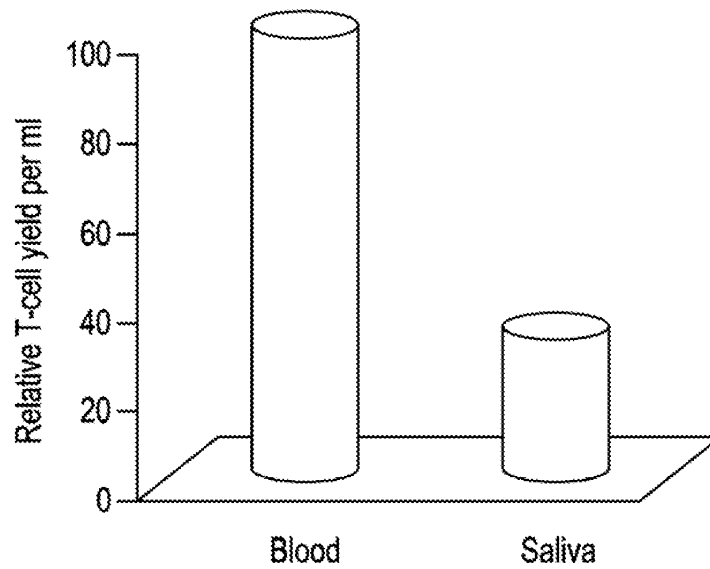


FIG. 10

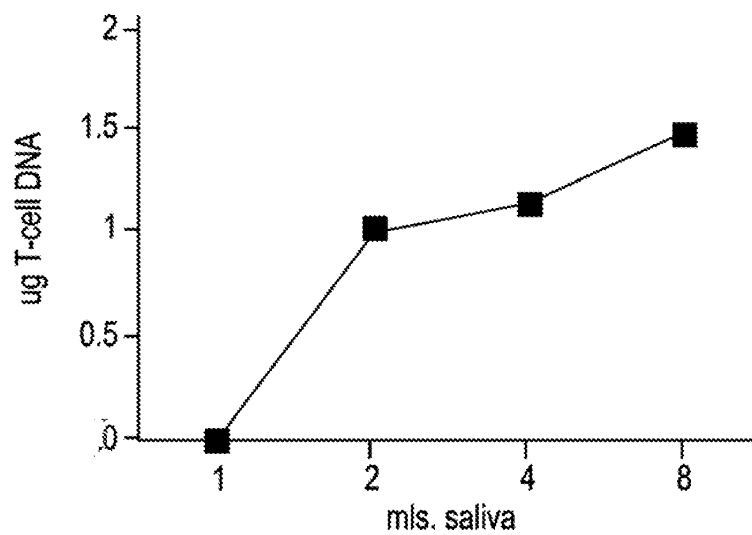


FIG. 7A

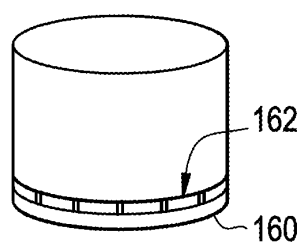


FIG. 7B

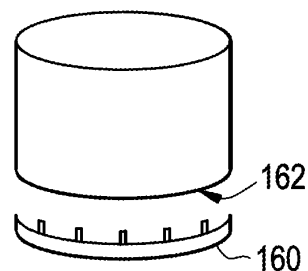
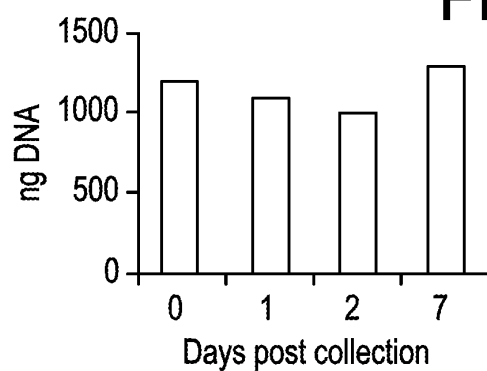


FIG. 8



Time course of DNA yield of isolated T-cells after saliva samples stored in preservation solution at room temperature and then proceed.



DNA extracted from isolated T-cells after stored in preservation solution for indicated time.

FIG. 9

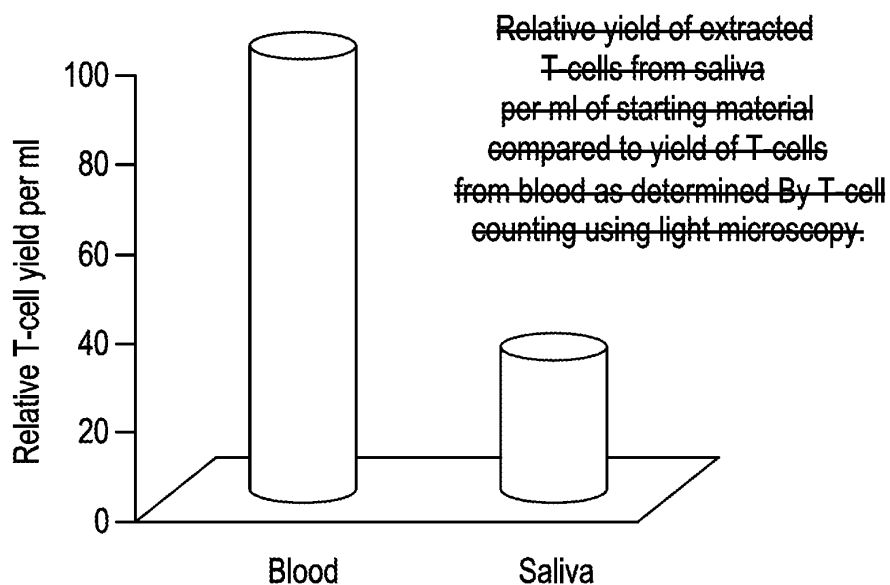
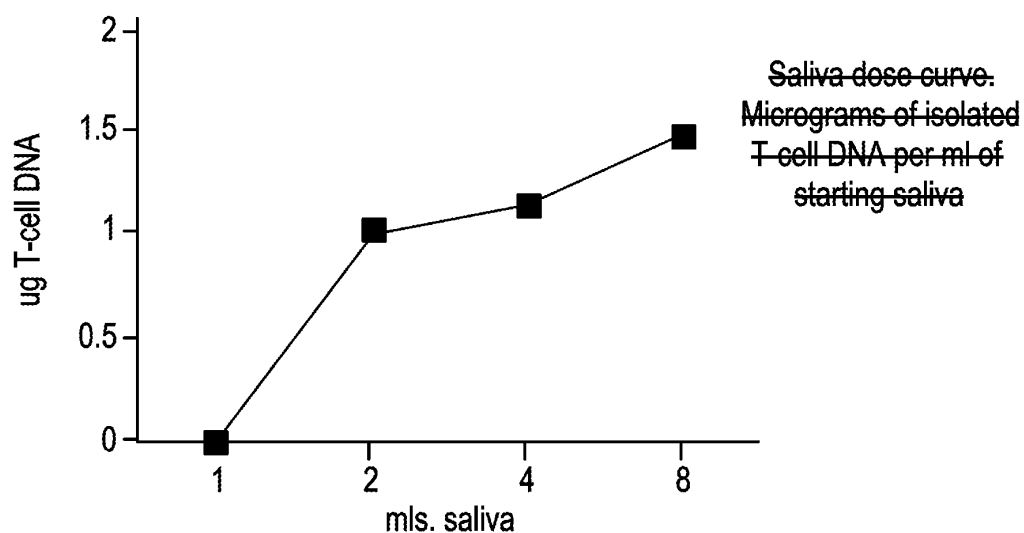


FIG. 10



Docket No.: OSHH-001/C05US 158166-2025
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor: Youssef BIADILLAH Confirmation No.: 3950
Application No.: 17/510,003 Group Art Unit: TBD
Filed: October 25, 2021 Examiner: TBD
For: BIOLOGICAL COLLECTION SYSTEM

Via EFS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO NOTICE TO FILE CORRECTED APPLICATION PAPERS

This paper is filed in response to the Notice to File Corrected Application Papers (“the Notice”) mailed November 4, 2021, in the above-identified patent application. Accordingly, this paper is timely filed on or before January 4, 2022. Prior to examination of the above-identified application, Applicant respectfully requests entry of the following amendments.

Amendment to Drawings begin on page 2 of this paper.

Amendments to the Specification begin on page 3 of this paper.

Remarks begin on page 4 of this paper.

AMENDMENTS TO THE DRAWINGS

Please replace originally filed Drawing Sheets 8 of 9 and 9 of 9 with the attached Replacement Sheets (both marked-up and clean versions) in compliance with 37 C.F.R. §§1.84 and 37 C.F.R. §1.21(d).

No new matter is added.

AMENDMENTS TO THE SPECIFICATION

Please replace the originally filed specification (excluding the claims and the Abstract), with the Substitute Specification submitted herewith (both marked-up and clean versions), in compliance with 37 CFR 1.121(b)(3) and 1.125. No new matter is added.

REMARKS

In the Notice to file corrected application papers, the Office states that FIGS. 8-10 contain excessive text.

In response, Applicant submits herewith replacement sheets where the excessive text in FIGS. 8-10 is removed.

The excessive text of FIGS. 8-9 is moved to the section of BRIEF DESCRIPTION OF THE DRAWINGS in the substitute specification submitted herewith.

The excessive text in FIG. 10 is duplicative of the description in paragraph [0055] of the specification as filed. Accordingly, the excessive text in FIG. 10 is not included in the substitute specification submitted herewith.

Application No.: 17/510,003

Docket No.: OSHH-001/C05US 158166-2025

CONCLUSION

In view of the foregoing, Applicant respectfully submits that no further impediments exist to the allowance of this application and, therefore, requests an indication of allowability. However, the Examiner is requested to call the undersigned if any questions or comments arise.

The Director is hereby authorized to charge any appropriate fees under 37 C.F.R. §§1.16, 1.17, and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 50-1283 **referencing Docket No. OSHH-001/C05US 158166-2025.**

Dated: January 4, 2022

Respectfully submitted,
COOLEY LLP

USPTO CUSTOMER NO. 58249

COOLEY LLP
ATTN: IP Docketing Department
1299 Pennsylvania Avenue NW, Suite 700
Washington, DC 20004

By: /Chun L. Yu/
(Chris) Chun L. Yu, Ph.D.
Reg. No. 68,138

Tel: (212) 479-6463
Fax: (212) 479-6275



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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO	TOT CLAIMS	IND CLAIMS
17/510,003	10/25/2021		1820	OSHH-001C05US 158166-2025	20	1

CONFIRMATION NO. 3950
UPDATED FILING RECEIPT



CC000000130924083

58249
COOLEY LLP
ATTN: IP Docketing Department
1299 Pennsylvania Avenue, NW
Suite 700
Washington, DC 20004

Date Mailed: 01/07/2022

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Inventor(s)

Youssef BIADILLAH, Geneva, SWITZERLAND;
Stephen D. ANDREWS, Falmouth, ME;

Applicant(s)

DNA GENOTEK, INC., Ottawa, CANADA;

Assignment For Published Patent Application

DNA GENOTEK, INC., Ottawa, CANADA

Power of Attorney: None

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which is a CON of 15/227,693 08/03/2016 ABN
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Projected Publication Date: 04/14/2022

Non-Publication Request: No

Early Publication Request: Yes

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BIOLOGICAL COLLECTION SYSTEM

Preliminary Class

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NOT GRANTED

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/510,003	10/25/2021	Youssef BIADILLAH	OSHH-001C05US 158166-2025	3950
58249	7590	01/25/2022	EXAMINER	
COOLEY LLP			CENTRAL, DOCKET	
ATTN: IP Docketing Department			ART UNIT	
1299 Pennsylvania Avenue, NW			PAPER NUMBER	
Suite 700			1797	
Washington, DC 20004			NOTIFICATION DATE	
			DELIVERY MODE	
			01/25/2022	
			ELECTRONIC	

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

zIPPatentDocketingMailboxUS@cooley.com

<i>Decision Granting Request for Prioritized Examination (Track I)</i>	Application No. 17/510,003	Applicant(s) BIADILLAH et al.	
	Examiner DIANE C GOODWYN	Art Unit OPET	AIA (FITF) Status No
1. THE REQUEST FILED <u>25 October 2021</u> IS <u>GRANTED</u> . The above-identified application has met the requirements for prioritized examination A. ☒ for an original nonprovisional application (Track I). B. ☐ for an application undergoing continued examination (RCE). 2. The above-identified application will undergo prioritized examination. The application will be accorded special status throughout its entire course of prosecution until one of the following occurs: A. filing a <u>petition for extension of time</u> to extend the time period for filing a reply; B. filing an <u>amendment to amend the application to contain more than four independent claims, more than thirty total claims</u>, or a multiple dependent claim; C. filing a <u>request for continued examination</u> ; D. filing a notice of appeal; E. filing a request for suspension of action; F. mailing of a notice of allowance; G. mailing of a final Office action; H. completion of examination as defined in 37 CFR 41.102; or I. abandonment of the application. Telephone inquiries with regard to this decision should be directed to DIANE GOODWYN at (571) 272-6735. In his/her absence, calls may be directed to Petition Help Desk at (571) 272-3282.			
/DIANE C GOODWYN/ Paralegal Specialist, OPET			



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17/510,003	10/25/2021	Youssef BIADILLAH	OSHH-001C05US 158166-2025

CONFIRMATION NO. 3950

PUBLICATION NOTICE



OC000000133172626*

58249
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Title: BIOLOGICAL COLLECTION SYSTEM

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Publication Date: 04/14/2022

NOTICE OF PUBLICATION OF APPLICATION

The above-identified application will be electronically published as a patent application publication pursuant to 37 CFR 1.211, et seq. The patent application publication number and publication date are set forth above.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/510,003	10/25/2021	Youssef BIADILLAH	OSHH-001C05US 158166-2025	3950
58249	7590	05/03/2022	EXAMINER	
COOLEY LLP			SIEFKE, SAMUEL P	
ATTN: IP Docketing Department			ART UNIT	PAPER NUMBER
1299 Pennsylvania Avenue, NW				
Suite 700			1797	
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			05/03/2022	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

zIPPatentDocketingMailboxUS@cooley.com

DETAILED ACTION

Notice of Pre-AIA or AIA Status

The present application is being examined under the pre-AIA first to invent provisions.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112(a):

(a) IN GENERAL.—The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

The following is a quotation of the first paragraph of pre-AIA 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 6 is rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor or a joint inventor, or for applications subject to pre-AIA 35 U.S.C. 112, the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 6 requires the second cylinder comprises a plurality of vents. A plurality of vents is not disclosed in the specification or disclosed in the drawings. A single aperture (20) is seen in figure 3a,3b.

The following is a quotation of 35 U.S.C. 112(b):

(b) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-20 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor (or for applications subject to pre-AIA 35 U.S.C. 112, the applicant), regards as the invention.

Claim 1 recites the limitation "a connection member" in line 9. There is insufficient antecedent basis for this limitation in the claim. There are two "connection member" present in claim 1 which are directed to different structures. Applicant needs to rename one of the connection member to clarify the claim. Suggested examples, first connection member, second connection member complementary to the first connection member; first coupling feature, second coupling feature complementary to the first coupling feature.

Claim 1 recites the limitation "an aperture" in line 5, 7, 14. There is insufficient antecedent basis for this limitation in the claim. There are two "an aperture" structures present in claim 1. Applicant needs to clarify and distinguish between the three apertures. Suggested examples, first aperture, second aperture, third aperture.

Claim 7-8 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor (or for applications subject to pre-AIA 35 U.S.C. 112, the applicant), regards as the invention. Claim 7 requires the annular valve comprise a flange. It is unclear if the flange is attached to the first cylinder or the second cylinder. The specification gives support to the flange is part of the first cylinder as shown in fig. 3a, 3b (flange 48, first cylinder 62). It is suggested that Applicant recite the flange being a part of the first cylinder.

Allowable Subject Matter

Claims 1-20 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The prior art does not teach or fairly suggest a biological sample collection system, the system comprising: a sample collection vessel comprising a sample collection reservoir, a connection member, and an aperture for receiving a biological sample; a cap comprising an aperture, a reagent chamber storing a reagent therein, and a connection member complementary to the connection member of the sample collection vessel; and a moveable annular valve in the aperture of the cap, the moveable annular valve comprising a vent, a first cylinder comprising an aperture, a second cylinder comprising the vent, the second cylinder positioned in the aperture of the first cylinder, a closed configuration, and an open configuration, wherein in the annular valve's closed configuration, the first and second cylinders create a fluid-tight seal with the cap and the first cylinder obstructs the vent to retain the reagent in the

reagent chamber, the first cylinder and second cylinder are relatively moveable to thereby change the annular valve from the closed configuration to the open configuration, and in the annular valve's open configuration, the first cylinder does not obstruct the vent to thereby allow flow of the reagent from the reagent chamber, through the vent, and into the sample collection reservoir.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAMUEL P SIEFKE whose telephone number is (571)272-1262. The examiner can normally be reached Monday, Tuesday, Thursday, Friday, 8-6.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at <http://www.uspto.gov/interviewpractice>.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lyle Alexander can be reached on 571-272-1254. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: <https://patentcenter.uspto.gov>. Visit <https://www.uspto.gov/patents/apply/patent->

Application/Control Number: 17/510,003
Art Unit: 1797

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/SAMUEL P SIEFKE/
Primary Examiner, Art Unit 1797

Search Notes 	Application/Control No. 17/510,003	Applicant(s)/Patent Under Reexamination BIADILLAH et al.
	Examiner SAMUEL P SIEFKE	Art Unit 1797

CPC - Searched*		
Symbol	Date	Examiner
(G01N1/30 or A61B10/0051 or A61B10/007 or A61B10/0096 or B01L3/502 or G01N1/10 or B01L3/5021 or B01L3/50825 or B01L2200/025 or B01L2200/0689 or B01L2200/085 or B01L2300/042 or B01L2300/047 or B01L2300/049 or B01L2300/0832 or B01L2400/0683 or G01N2001/002 or G01N2001/305 or A01N1/0273 or A01N1/0226 or G01N1/28 or C12N2509/10 or C12N5/0636).cpc.	04/28/2022	

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
East search attached	04/28/2022	SS

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor: Youssef BIADILLAH Confirmation No.: 3950
Application No.: 17/510,003 Group Art Unit: 1797
Filed: October 25, 2021 Examiner: Not Yet Assigned
For: BIOLOGICAL COLLECTION SYSTEM

Via EFS
Commissioner for Patents
Alexandria, VA 22313-1450

AMENDMENT/RESPONSE TO OFFICE ACTION

In response to the Non-Final Office Action dated May 3, 2022 (“Final Office Action”, “Office Action”, or “Action”), to which the deadline for responding is August 3, 2022, Applicant submits the following Amendments and Remarks, and respectfully requests reconsideration of the application in view thereof.

Any extensions of time necessary to prevent abandonment of this application are hereby petitioned for under 37 C.F.R. §1.136(a), and any additional fees required (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 50-1283.

Amendments to the Claims begin on page 2.

Remarks begin on page 7.

Amendments to the Claims

The following listing of the claims listing replaces all prior listing and provides all amendments, new claims, and claim cancelations by this Response.

1. **(Currently Amended)** A biological sample collection system, the system comprising:
 - a sample collection vessel comprising
 - a sample collection reservoir,
 - a first connection member, and
 - [[an]] a first aperture for receiving a biological sample;
 - a cap comprising
 - [[an]] a second aperture,
 - a reagent chamber storing a reagent therein, and
 - a second connection member complementary to the first connection member ~~of the sample collection vessel~~; and
 - a moveable annular valve in the second aperture ~~of the cap~~, the moveable annular valve comprising
 - a vent,
 - a first cylinder comprising [[an]] a third aperture,
 - a second cylinder comprising the vent, the second cylinder positioned in the third aperture ~~of the first cylinder~~,
 - a closed configuration, and
 - an open configuration, wherein
 - in the annular valve's closed configuration, the first and second cylinders create a fluid-tight seal with the cap and the first cylinder obstructs the vent to retain the reagent in the reagent chamber,

the first cylinder and second cylinder are relatively moveable to thereby change the annular valve from the closed configuration to the open configuration, and

in the annular valve's open configuration, the first cylinder does not obstruct the vent to thereby allow flow of the reagent from the reagent chamber, through the vent, and into the sample collection reservoir.

2. (Previously Presented) The biological sample collection system of claim 1, wherein the second cylinder comprises a sidewall and the sidewall comprises the vent, wherein the annular valve's closed configuration comprises a sidewall of the first cylinder obstructing the vent and the annular valve's open configuration comprises the sidewall of the first cylinder not obstructing the vent.
3. (Previously Presented) The biological sample collection system of claim 1, wherein the first and second cylinder's relative movement, from the annular valve's closed configuration to the open configuration, is translational along a longitudinal axis of the cap.
4. **(Currently Amended)** The biological sample collection system of claim 1, wherein the first and second cylinder's relative movement, from the annular valve's closed configuration to the open configuration, comprises the second cylinder moving in the third aperture ~~of the first cylinder~~.
5. (Previously Presented) The biological sample collection system of claim 1, wherein the first cylinder comprises a press-fit connection with the cap.

6. (Previously Presented) The biological sample collection system of claim 1, wherein the second cylinder comprises a plurality of vents and the first cylinder obstructs the plurality of vents in the annular valve's closed configuration.
7. **(Currently Amended)** The biological sample collection system of claim 1, wherein the first cylinder of the annular valve comprises a flange and the annular valve with flange comprises a width larger than a width of the ~~collection vessel's~~ first aperture.
8. (Previously Presented) The biological sample collection system of claim 7, wherein interaction between the flange and a wall of the sample collection vessel causes the first and second cylinders to move relatively and change the annular valve from the closed configuration to the open configuration.
9. (Previously Presented) The biological sample collection system of claim 1, further comprising a funnel attachable to the sample collection vessel
10. (Previously Presented) The biological sample collection system of claim 1, wherein the vent is at least partially unobstructed in the annular valve's open configuration.
11. (Previously Presented) The biological sample collection system of claim 1, wherein the vent is fully unobstructed in the annular valve's open configuration.
12. (Previously Presented) The biological sample collection system of claim 1, wherein the first and second cylinders comprise generally constant exterior diameters.

13. (Previously Presented) The biological sample collection system of claim 12, wherein the annular valve comprises a flange extending from at least one of the first and second cylinders.
14. **(Currently Amended)** The biological sample collection system of claim 1, wherein the first and second connection members comprise a threaded connection.
15. (Previously Presented) The biological sample collection system of claim 1, wherein the annular valve comprises a sliding connection between the first and second cylinders.
16. (Previously Presented) The biological sample collection system of claim 1, wherein the sample collection system comprises a separable two-piece sample collection system, the sample collection vessel comprising a first piece of the separable two-piece sample collection system, and the cap with movable annular valve comprising a second piece of the separable two-piece sample collection system.
17. (Previously Presented) The biological sample collection system of claim 1, wherein the first cylinder comprises threads on an interior sidewall configured to mate with threads on an exterior sidewall of the second cylinder.
18. (Previously Presented) The biological sample collection system of claim 1, wherein a diameter of an inner wall of the first cylinder is sufficiently equal to a diameter of an outer wall of the second cylinder to create a fluid-tight connection therebetween and allow relative movement.

19. (Previously Presented) The biological sample collection system of claim 1, wherein the system is configured such that connecting the cap to the sample collection vessel causes the annular valve to move from the closed configuration to the open configuration.
20. (Previously Presented) The biological sample collection system of claim 1, wherein the system is configured such that connecting the cap to the sample collection vessel causes the annular valve to move from the closed configuration to the open configuration, wherein the second cylinder comprises a sidewall and the sidewall comprises the vent, wherein the annular valve's closed configuration comprises a sidewall of the first cylinder obstructing the vent and the annular valve's open configuration comprises the sidewall of the first cylinder not obstructing the vent, and wherein the first and second cylinder's relative movement, from the annular valve's closed configuration to the open configuration, is translational along a longitudinal axis of the cap.

REMARKS

Upon entry to these amendments, claims 1-20 are pending in the present application. In this response, claims 1, 4, 7, and 14 are amended. Support for the claim amendments can be found throughout the application as originally filed.

No new matter has been added. Amendment of certain claims is not to be construed as a dedication to the public of any of the subject matter of the claims as previously presented.

Applicant respectfully notes that the amendments made to the claims are being presented merely to expedite the prosecution and allowance of the subject application and not as an admission or agreement with the Office's allegations of unpatentability as previously presented. Moreover, arguments raised by Applicant in this and previous papers are applicable only as to those specific embodiments to which such arguments were submitted. Applicant reserves the right to pursue claims directed to the previously presented claimed embodiments, the embodiments recited in the original claims, as well as any other embodiments supported by the present disclosure, in this or subsequent filings, including those which are broader in scope than the present and original claims.

Claim Rejections – 35 USC §112

The Examiner rejected claim 6 under 35 USC 112(a) or 35 USC 112(pre-AIA), first paragraph, as allegedly failing to comply with the written description requirement. The Application respectfully disagrees with this assessment. The Applicant respectfully submits that the claimed embodiment is implicitly supported by the application as filed. It would be obvious to have more than one vent and difficult to depict multiple vents in a cross-sectional drawing. Withdrawal of this rejection is respectfully requested.

The Examiner has rejected claims 1-20 under 35 USC 112(b) or 35 USC 112 (pre-AIA), second paragraph, as allegedly being indefinite. Claims 1 and 7 have been amended in accordance with the Examiner's suggestions, thus rendering this rejection moot. Clarifying amendments have been made to claims 4, 7, and 14 in view of the amendments to claim 1. Withdrawal of this rejection is respectfully requested.

CONCLUSION

Applicant respectfully submits that all of the issues raised in the Non-Final Action of May 3, 2022 have been addressed. **IF THERE ARE ANY QUESTIONS REGARDING THIS RESPONSE, THE EXAMINER IS ENCOURAGED TO CONTACT APPLICANT'S UNDERSIGNED REPRESENTATIVES AT THE TELEPHONE NUMBER PROVIDED BELOW.**

While the amendments and remarks are believed to be sufficient to overcome the Examiner's rejections, any omissions as to assertions by the Examiner or certain requirements that may be applicable to such rejections (e.g., assertions regarding dependent claims, whether a reference constitutes prior art, whether references are legally combinable for obviousness purposes) is not an admission that such assertions are accurate or such requirements have been met. Applicant reserves the right to analyze and dispute such positions in the future. In addition, failure of Applicant to address a specific rejection, issue or comment, from the outstanding Action, or any prior USPTO paper, does not signify agreement with or concession of such rejection, issue or comment. In addition, the arguments made the current paper are not intended to be exhaustive, as there may be reasons for patentability of any or all pending claims (or other claims) that have not been expressed herein. Finally, nothing in this paper, or in any prior response or communication filed by Applicant, should be construed as intent to concede any issue with regard to any claim, except as specifically stated.

Applicant does not concede that previously pending claims in this application are not patentable over the cited references. Rather, any amendments or characterizations are being made to expedite the issuance. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that relate to subject matter supported by the instant application, including subject matter specifically disclaimed herein (with respect to the currently claimed embodiments) or by any prior prosecution. Accordingly, reviewers of this application, or any parent, child or related prosecution history should not infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the instant application.

Application No.: 17/510,003

Docket No.: OSHH-001/C05US 158166-2025

The Director is hereby authorized to charge any appropriate fees under 37 C.F.R. §§1.16, 1.17, and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 50-1283 **referencing Docket No. OSHH-001/C05US 158166-2025.**

Dated: August 3, 2022

Respectfully submitted,
COOLEY LLP

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Electronic Patent Application Fee Transmittal				
Application Number:		17510003		
Filing Date:		25-Oct-2021		
Title of Invention:		BIOLOGICAL COLLECTION SYSTEM		
First Named Inventor/Applicant Name:		Youssef BIADILLAH		
Filer:		Mengran Liu/Grace Colucci		
Attorney Docket Number:		OSHH-001C05US 158166-2025		
Filed as Large Entity				
Filing Fees for Utility under 35 USC 111(a)				
Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD(\$)
Miscellaneous:				
SUBMISSION- INFORMATION DISCLOSURE STMT	1806	1	260	260
Total in USD (\$)				260

Electronic Acknowledgement Receipt	
EFS ID:	46330635
Application Number:	17510003
International Application Number:	
Confirmation Number:	3950
Title of Invention:	BIOLOGICAL COLLECTION SYSTEM
First Named Inventor/Applicant Name:	Youssef BIADILLAH
Customer Number:	58249
Filer:	Mengran Liu/Grace Colucci
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Receipt Date:	03-AUG-2022
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Payment was successfully received in RAM	\$260
RAM confirmation Number	E202283G30302392
Deposit Account	501283
Authorized User	Grace Colucci
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows: 37 CFR 1.16 (National application filing, search, and examination fees) 37 CFR 1.17 (Patent application and reexamination processing fees)	

37 CFR 1.19 (Document supply fees)					
37 CFR 1.20 (Post Issuance fees)					
37 CFR 1.21 (Miscellaneous fees and charges)					
File Listing:					
Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Foreign Reference	DE10219117C1_Stefan_CertifiedEnglishTranslation.pdf	3110565	no	9
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Warnings:					
Information:					
2	Foreign Reference	EP0215735A1wMachineEnglTranslation.pdf	7962927	no	35
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7	Foreign Reference	WO9217110A1.pdf	1353940	no	37
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Information:					

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Information:					
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Warnings:					
Information:					

28	Information Disclosure Statement (IDS) Form (SB08)	OSHH-001_C05US_sb08.pdf	283723	no	6
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Warnings:					
Information:					
This is not an USPTO supplied IDS fillable form					
29	Transmittal Letter	OSHH-001_C05US_158166-2025_IDS-Transmittal.pdf	109195	no	3
			d81112a2a9f8a28c1a2f4701a3fa955dc8e48d30		
Warnings:					
Information:					
30		OSHH-001-C05US_158166-2025_ResponseToNFOA.pdf	157567	yes	9
			1a77b17125fb7839046d26256f2e41101303531c		
	Multipart Description/PDF files in .zip description				
	Document Description		Start	End	
	Amendment/Request for Reconsideration-After Non-Final Rejection		1	1	
	Claims		2	6	
	Applicant Arguments/Remarks Made in an Amendment		7	9	
Warnings:					
Information:					
31	Fee Worksheet (SB06)	fee-info.pdf	37703	no	2
			6cde609c954b42a89c6f63d273af2b10ccbc58b1		
Warnings:					
Information:					
Total Files Size (in bytes):			139041565		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor: Youssef BIADILLAH Confirmation No.: 3950
Application No.: 17/510,003 Group Art Unit: 1797
Filed: October 25, 2021 Examiner: S. P. Siefke
For: BIOLOGICAL COLLECTION SYSTEM

Via EFS
Commissioner for Patents
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT
UNDER 37 C.F.R. §§ 1.56, 1.97, AND 1.98

In accordance with the duty of disclosure set forth in 37 C.F.R. §1.56, Applicant hereby submits the following information in conformance with 37 C.F.R. §§1.97 and 1.98. It is respectfully requested that the information be expressly considered during the prosecution of this application, and the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

The Applicant would like to bring to the Examiner's attention the enclosed documents in connection with ongoing litigation between Applicant and Spectrum Solutions L.L.C. before the United States District Court for the Southern District of California (DNA Genotek Inc. v. Spectrum Solutions L.L.C., USDC S.D. Cal., Case No. 21-cv-0516). This litigation concerns the following U.S. Patents: U.S. Patent No. 10,619,187 and U.S. Patent No. 11,002,646.

☒ Pursuant to 37 C.F.R. §1.98, a copy of each non-US patent document cited on the attached Form used in lieu of PTO/SB/08 is enclosed.

☐ No copies of the foreign patent, foreign patent application, or non-patent literature publications listed on the attached Form used in lieu of PTO/SB/08 are being provided pursuant to 37 C.F.R. §1.98(d) because the publications were previously

cited by or submitted to the Office in prior Application Serial No(s). _____ to which the above-identified application claims priority under 35 U.S.C. §120.

- ☐ No copies of any U.S. patents or U.S. patent application publications listed on the attached Form used in lieu of PTO/SB/08 are being provided pursuant to 37 C.F.R. §1.98.
- ☐ Publication(s) listed on the attached Form used in lieu of PTO/SB/08 were cited in a foreign search or examination report corresponding to application serial no. _____ and mailed on _____.
- ☐ Enclosed is a copy of a non-English publication(s) _____. Pursuant to §609 of the M.P.E.P., Applicant submits the attached foreign search or examination report, which cites such non-English language publication(s).
- ☐ Enclosed is a copy of a non-English publication(s) _____ English language publication _____ (copy enclosed) claims priority from this non-English publication.
- ☐ Enclosed is an explanation of non-English publication(s) _____ for which an English translation is not available.
- ☐ Enclosed is an English translation of non-English publication(s) _____ cited on the attached Form used in lieu of PTO/SB/08.
- ☐ Enclosed is an English language Abstract of non-English publication(s) _____ cited on the attached Form used in lieu of PTO/SB/08.
- ☐ Enclosed is a copy of pending patent Application No. _____.

[X] In accordance with **37 C.F.R. §1.97(c)**, this Information Disclosure Statement is filed after the period specified in 37 C.F.R. § 1.97(b), but before the mailing of any of the following: a final action under 37 C.F.R. §1.113; a notice of allowance under 37 C.F.R. §1.311; or an action that otherwise closes prosecution in this application.

In accordance with 37 C.F.R. §1.97(c) also enclosed is:

- [X] Fee under 37 C.F.R. §1.17(p) in the amount of \$260.00;
- ☐ Fee under 37 C.F.R. §1.17(p) in the amount of \$130.00;
- ☐ Fee under 37 C.F.R. §1.17(p) in the amount of \$65.00; or
- ☐ Statement as specified in 37 C.F.R. §1.97(e):
 - ☐ Each item of information contained in the Information Disclosure Statement cited herein was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing date of the Information Disclosure Statement; or
 - ☐ No item of information contained in the Information Disclosure Statement submitted herewith was cited in any communication from a foreign patent

office in a counterpart foreign application, and, to the knowledge of the undersigned, having made a reasonable inquiry, no item of information contained in the Information Disclosure Statement was known to any individual designated in 37 C.F.R. §1.56(c) more than three months prior to the filing date of the Information Disclosure Statement.

Remarks

In accordance with:

- 37 C.F.R. § 1.97(g), this Information Disclosure Statement shall not be construed as to mean that a search has been made; and
- 37 C.F.R. § 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in the statement is, or is considered to be material to patentability as defined by 37 C.F.R § 1.56(b).

It is respectfully requested that the Examiner consider the above-noted information and return an initialed copy of the attached Form used in lieu of PTO/SB/08 to the undersigned. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application. The Director is hereby authorized to charge any additional fees which may be required with respect to this communication, or credit any overpayment, to Deposit Account No. 50-1283, under Order No. OSHH-001/C05US 158166-2025.

Dated: August 25, 2022

Respectfully submitted,
COOLEY LLP

COOLEY LLP
ATTN: IP Docketing Department
1299 Pennsylvania Avenue NW, Suite 700
Washington, DC 20004
Tel: (617) 937-2300
Fax: (617) 937-2400

By: /Mengran Liu/
Mengran Liu
Reg. No. 80,682
Brian P. Hopkins
Reg. No. 42,669

TERMINAL DISCLAIMER TO OBVIATE A DOUBLE PATENTING REJECTION OVER A "PRIOR" PATENT	Docket Number (Optional) OSHH-001/C05US 158166-2025
--	--

In re Application of: Youssef BIADILLAH et al.

Application No.: 17/510,003

Filed: October 25, 2021

For: BIOLOGICAL COLLECTION SYSTEM

The applicant, DNA GENOTEK, INC., owner of 100 percent interest in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of **prior patent** No. 11,002,646 as the term of said **prior patent** is presently shortened by any terminal disclaimer. The applicant hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the **prior patent** are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

In making the above disclaimer, the applicant does not disclaim the terminal part of the term of any patent granted on the instant application that would extend to the expiration date of the full statutory term of the **prior patent**, "as the term of said **prior patent** is presently shortened by any terminal disclaimer," in the event that said **prior patent** later:

- expires for failure to pay a maintenance fee;
- is held unenforceable;
- is found invalid by a court of competent jurisdiction;
- is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321;
- has all claims canceled by a reexamination certificate;
- is reissued; or
- is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.

Check either box 1 or 2 below, if appropriate.

1. ☐ The undersigned is the applicant. If the applicant is an assignee, the undersigned is authorized to act on behalf of the assignee.

I hereby acknowledge that any willful false statements made are punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

2. ☒ The undersigned is an attorney or agent of record. Reg. No. 80,682

/Mengran Liu/
Signature

Mengran Liu
Typed or printed name

Attorney for Applicant(s)
Title

August 25, 2022
Date

(617) 937-2300
Telephone Number

☒ Terminal disclaimer fee under 37 CFR 1.20(d) included.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

Application Number * 17/510,003 *	Application/Control No. 17/510,003	Applicant(s)/Patent under Reexamination BIADILLAH et al.	
	Examiner SIEFKE, SAMUEL P	Art Unit 1797	
Document Code - DISQ		Internal Document - DO NOT MAIL	

TERMINAL DISCLAIMER	☐ APPROVED	☒ DISAPPROVED
Date Filed: <u>25 August 2022</u>	This patent is subject to a Terminal Disclaimer	

Approved/Disapproved by: /JEAN PROCTOR/ Technology Center: <u>OPLC</u> Telephone: <u>(571)272-1040</u> <u>The person who signed the terminal disclaimer (only for applications filed on or after September 16, 2012 is not the applicant, patentee or an attorney or agent of record. 37 CFR 1.321(a) and (b). (See FP 14.26.08) failed to state his/her capacity to sign for the juristic entity, and he/she has not been established as being authorized to act on behalf of the applicant. (See FP 14.26.09).</u> <u>(Note: PoA can be given to customer number, wherein all practitioners listed under the customer number have PoA. If PoA is given to a list of practitioners by registration number, the list may not comprise more than 10 practitioners or a separate paper signed by a 37 CFR 1.33(b) party must be in the record identifying which of the practitioners, up to 10, are recognized as having PoA. If the applicant is a juristic entity (e.g., corporation), a representative of the applicant cannot sign the TD unless it is established that the representative is a party authorized to act on behalf of the applicant.)</u>



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

58249 7590 09/07/2022
COOLEY LLP
ATTN: IP Docketing Department
1299 Pennsylvania Avenue, NW
Suite 700
Washington, DC 20004

EXAMINER

SIEFKE, SAMUEL P

ART UNIT

PAPER NUMBER

1797

DATE MAILED: 09/07/2022

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/510,003	10/25/2021	Youssef BIADILLAH	OSHH-001C05US 158166-2025	3950

TITLE OF INVENTION: BIOLOGICAL COLLECTION SYSTEM

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1200	\$0.00	\$0.00	\$1200	12/07/2022

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Maintenance fees are due in utility patents issuing on applications filed on or after Dec. 12, 1980. It is patentee's responsibility to ensure timely payment of maintenance fees when due. More information is available at www.uspto.gov/PatentMaintenanceFees.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via EFS-Web.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

58249 7590 09/07/2022
COOLEY LLP
ATTN: IP Docketing Department
1299 Pennsylvania Avenue, NW
Suite 700
Washington, DC 20004

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via EFS-Web or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/510,003	10/25/2021	Youssef BIADILLAH	OSHH-001C05US 158166-2025	3950

TITLE OF INVENTION: BIOLOGICAL COLLECTION SYSTEM

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1200	\$0.00	\$0.00	\$1200	12/07/2022

EXAMINER	ART UNIT	CLASS-SUBCLASS
SIEFKE, SAMUEL P	1797	422-568000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,

1 _____

(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. Fees submitted: ☐ Issue Fee ☐ Publication Fee (if required) ☐ Advance Order - # of Copies _____

4b. Method of Payment: (Please first reapply any previously paid fee shown above)

☐ Electronic Payment via EFS-Web ☐ Enclosed check ☐ Non-electronic payment by credit card (Attach form PTO-2038)

☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. _____

5. Change in Entity Status (from status indicated above)

☐ Applicant certifying micro entity status. See 37 CFR 1.29

☐ Applicant asserting small entity status. See 37 CFR 1.27

☐ Applicant changing to regular undiscounted fee status.

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment. NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____

Date _____

Typed or printed name _____

Registration No. _____



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/510,003	10/25/2021	Youssef BIADILLAH	OSHH-001C05US ~~158166-2025~~	3950
58249	7590	09/07/2022	EXAMINER SIEFKE, SAMUEL P	
COOLEY LLP ATTN: IP Docketing Department 1299 Pennsylvania Avenue, NW Suite 700 Washington, DC 20004			ART UNIT 1797	
DATE MAILED: 09/07/2022				

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b) (2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 17/510,003	Applicant(s) BIADILLAH et al.	
	Examiner SAMUEL P SIEFKE	Art Unit 1797	AIA (FITF) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 8/3/22.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

3. ☒ The allowed claim(s) is/are 1-20. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a) ☐ All b) ☐ Some* c) ☐ None of the:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.

☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892) 2. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____. 3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____. 4. ☒ Interview Summary (PTO-413), Paper No./Mail Date _____. /SAMUEL P SIEFKE/ Primary Examiner, Art Unit 1797	5. ☐ Examiner's Amendment/Comment 6. ☒ Examiner's Statement of Reasons for Allowance 7. ☐ Other _____
---	---

DETAILED ACTION

Notice of Pre-AIA or AIA Status

The present application is being examined under the pre-AIA first to invent provisions.

Allowable Subject Matter

Claims 1-20 are allowed.

The following is an examiner's statement of reasons for allowance: See the reasons for allowability in the Non-Final Office action dated 5/3/22.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAMUEL P SIEFKE whose telephone number is (571)272-1262. The examiner can normally be reached Monday, Tuesday, Thursday, Friday, 8-6.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an

interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at <http://www.uspto.gov/interviewpractice>.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lyle Alexander can be reached on 571-272-1254. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: <https://patentcenter.uspto.gov>. Visit <https://www.uspto.gov/patents/apply/patent-center> for more information about Patent Center and <https://www.uspto.gov/patents/docx> for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SAMUEL P SIEFKE/
Primary Examiner, Art Unit 1797

<i>Examiner-Initiated Interview Summary</i>	Application No. 17/510,003	Applicant(s) BIADILLAH et al.		
	Examiner SAMUEL P SIEFKE	Art Unit 1797	AIA (First Inventor to File) Status No	Page 1 of 1

All Participants (applicant, applicants representative, PTO personnel)	Title	Type
SAMUEL P SIEFKE	Primary Examiner	Telephonic
Mengran Liu	Attorney of Record	

Date of Interview: 22 August 2022

Issues Discussed:

Non-statutory Double Patenting

Applicant was informed a terminal disclaimer would be needed to overcome an Obvious double Patenting over US 11,002,646. Applicant stated a Terminal Disclaimer would be filed along with an IDS.

/SAMUEL P SIEFKE/ Primary Examiner, Art Unit 1797	
Applicant is reminded that a complete written statement as to the substance of the interview must be made of record in the application file. It is the applicants responsibility to provide the written statement, unless the interview was initiated by the Examiner and the Examiner has indicated that a written summary will be provided. See MPEP 713.04 Please further see: MPEP 713.04 Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews, paragraph (b) 37 CFR § 1.2 Business to be transacted in writing	

Applicant recordation instructions: It is not necessary for applicant to provide a separate record of the substance of interview.

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

<i>Search Notes</i> 	Application/Control No. 17/510,003	Applicant(s)/Patent Under Reexamination BIADILLAH et al.
	Examiner SAMUEL P SIEFKE	Art Unit 1797

CPC - Searched*		
Symbol	Date	Examiner
(G01N1/30 or A61B10/0051 or A61B10/007 or A61B10/0096 or B01L3/502 or G01N1/10 or B01L3/5021 or B01L3/50825 or B01L2200/025 or B01L2200/0689 or B01L2200/085 or B01L2300/042 or B01L2300/047 or B01L2300/049 or B01L2300/0832 or B01L2400/0683 or G01N2001/002 or G01N2001/305 or A01N1/0273 or A01N1/0226 or G01N1/28 or C12N2509/10 or C12N5/0636).cpc.	04/28/2022	
(G01N1/30 or A61B10/0051 or A61B10/007 or A61B10/0096 or B01L3/502 or G01N1/10 or B01L3/5021 or B01L3/50825 or B01L2200/025 or B01L2200/0689 or B01L2200/085 or B01L2300/042 or B01L2300/047 or B01L2300/049 or B01L2300/0832 or B01L2400/0683 or G01N2001/002 or G01N2001/305 or A01N1/0273 or A01N1/0226 or G01N1/28 or C12N2509/10 or C12N5/0636).cpc.	08/19/2022	SS

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
East search attached	04/28/2022	SS
East search attached	08/19/2022	SS

--	--

<i>Search Notes</i> 	Application/Control No. 17/510,003	Applicant(s)/Patent Under Reexamination BIADILLAH et al.
	Examiner SAMUEL P SIEFKE	Art Unit 1797

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner
G01N	1/30	08/19/2022	SS

--	--

Issue Classification 	Application/Control No. 17/510,003	Applicant(s)/Patent Under Reexamination BIADILLAH et al.
	Examiner SAMUEL P SIEFKE	Art Unit 1797

CPC						
Symbol					Type	Version
G01N	/	1	/	30	F	2013-01-01
A61B	/	10	/	0051	I	2013-01-01
A61B	/	10	/	007	I	2013-01-01
A61B	/	10	/	0096	I	2013-01-01
B01L	/	3	/	502	I	2013-01-01
G01N	/	1	/	10	I	2013-01-01
G01N	/	2001	/	002	A	2013-01-01
B01L	/	3	/	5021	A	2013-01-01
B01L	/	3	/	50825	A	2013-01-01
B01L	/	2300	/	047	A	2013-01-01
B01L	/	2300	/	049	A	2013-01-01
B01L	/	2400	/	0683	A	2013-01-01
B01L	/	2200	/	025	A	2013-01-01
B01L	/	2200	/	0689	A	2013-01-01
B01L	/	2200	/	085	A	2013-01-01
B01L	/	2300	/	042	A	2013-01-01
B01L	/	2300	/	0832	A	2013-01-01
G01N	/	2001	/	305	A	2013-01-01

CPC Combination Sets					
Symbol	Type	Set	Ranking	Version	
/					

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	20	
/SAMUEL P SIEFKE/ Primary Examiner, Art Unit 1797	19 August 2022	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	3b

U.S. Patent and Trademark Office

Part of Paper No.: 20220819

Issue Classification 	Application/Control No. 17/510,003	Applicant(s)/Patent Under Reexamination BIADILLAH et al.
	Examiner SAMUEL P SIEFKE	Art Unit 1797

INTERNATIONAL CLASSIFICATION			
CLAIMED			
G01N		1	30

NON-CLAIMED			

US ORIGINAL CLASSIFICATION	
CLASS	SUBCLASS

CROSS REFERENCES(S)						
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)					

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	20	
/SAMUEL P SIEFKE/ Primary Examiner, Art Unit 1797 (Primary Examiner)	19 August 2022 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure 3b

U.S. Patent and Trademark Office

Part of Paper No.: 20220819

Issue Classification 	Application/Control No. 17/510,003	Applicant(s)/Patent Under Reexamination BIADILLAH et al.
	Examiner SAMUEL P SIEFKE	Art Unit 1797

☒ Claims renumbered in the same order as presented by applicant ☐ CPA ☒ T.D. ☐ R.1.47																
CLAIMS																
Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Original
	1		10		19											
	2		11		20											
	3		12													
	4		13													
	5		14													
	6		15													
	7		16													
	8		17													
	9		18													

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	20	
/SAMUEL P SIEFKE/ Primary Examiner, Art Unit 1797	19 August 2022	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	3b

U.S. Patent and Trademark Office

Part of Paper No.: 20220819

Bibliographic Data

Application No: 17/510,003

Foreign Priority claimed: ☐ Yes ☒ No

35 USC 119 (a-d) conditions met: ☐ Yes ☐ No ☐ Met After Allowance

Verified and Acknowledged: /SAMUEL P SIEFKE/

Examiner's Signature

Initials

Title: BIOLOGICAL COLLECTION SYSTEM

FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
10/25/2021	422	1797	OSHH-001C05US 158166-2025
RULE			

APPLICANTS

DNA GENOTEK, INC., Ottawa, CANADA

INVENTORS

Youssef BIADILLAH, Geneva, SWITZERLAND

Stephen D. ANDREWS, Falmouth, ME, UNITED STATES

CONTINUING DATA

This application is a CON of 16023772 06/29/2018

16023772 is a CON of 15227693 08/03/2016ABN

15227693 is a CON of 14127832 12/19/2013 PAT 9442046

14127832 is a 371 of PCT/US2012/043176 06/19/2012

PCT/US2012/043176 has PRO of 61598601 02/14/2012

PCT/US2012/043176 has PRO of 61598618 02/14/2012

PCT/US2012/043176 has PRO of 61498584 06/19/2011

FOREIGN APPLICATIONS

IF REQUIRED, FOREIGN LICENSE GRANTED**

11/03/2021

STATE OR COUNTRY

SWITZERLAND

ADDRESS

COOLEY LLP

ATTN: IP Docketing Department

1299 Pennsylvania Avenue, NW

Suite 700

Washington, DC 20004

UNITED STATES
FILING FEE RECEIVED
\$6,160

TRANSMITTAL FOR POWER OF ATTORNEY-IN-FACT TO ONE OR MORE REGISTERED PRACTITIONERS			
Application Number	17/510,003		
Filing Date	October 25, 2021		
First Named Inventor	Youssef BIADILLAH		
Title	BIOLOGICAL COLLECTION SYSTEM		
Art Unit	1797		
Examiner Name	S. P. Siefke		
Attorney Docket Number	OSHH-001/C05US 158166-2025		
SIGNATURE of Applicant or Patent Practitioner			
Signature	/Mengran Liu/	Date (Optional)	
Name	Mengran Liu	Registration Number	80,682
Title (if Applicant is a juristic entity)			
Applicant Name (if Applicant is a juristic entity)			
☐ *Total of <u>1</u> forms are submitted.			

POWER OF ATTORNEY-IN-FACT BY APPLICANT

I hereby revoke all previous powers of attorney given in the application identified in either the attached transmittal letter or the boxes below.

Application Number	Filing Date

(Note: The boxes above may be left blank if information is provided on form PTO/AIA/82A.)

☒ I hereby appoint the Patent Practitioner(s) associated with the following Customer Number as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the application referenced in the attached transmittal letter (form PTO/AIA/82A) or identified above:

58249

OR

☐ I hereby appoint Practitioner(s) named in the attached list (form PTO/AIA/82C) as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the patent application referenced in the attached transmittal letter (form PTO/AIA/82A) or identified above. (Note: Complete form PTO/AIA/82C.)

Please recognize or change the correspondence address for the application identified in the attached transmittal letter or the boxes above to:

☒ The address associated with the above-mentioned Customer Number

OR

☐ The address associated with Customer Number:

OR

☐ Firm or
Individual Name

Address

City

State

Zip

Country

Telephone

Email

I am the Applicant (if the Applicant is a juristic entity, list the Applicant name in the box):

DNA GENOTEK, INC.

☐ Inventor or Joint Inventor (title not required below)

☐ Legal Representative of a Deceased or Legally Incapacitated Inventor (title not required below)

☒ Assignee or Person to Whom the Inventor is Under an Obligation to Assign (provide signer's title if applicant is a juristic entity)

☐ Person Who Otherwise Shows Sufficient Proprietary Interest (e.g., a petition under 37 CFR 1.46(b)(2) was granted in the application or is concurrently being filed with this document) (provide signer's title if applicant is a juristic entity)

SIGNATURE of Applicant for Patent

The undersigned (whose title is supplied below) is authorized to act on behalf of the applicant (e.g., where the applicant is a juristic entity).

Signature

Date (Optional)

Name

Title

NOTE: Signature - This form must be signed by the applicant in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. If more than one applicant, use multiple forms.

☒ Total of 1 forms are submitted.

TERMINAL DISCLAIMER TO OBVIATE A DOUBLE PATENTING REJECTION OVER A "PRIOR" PATENT	Docket Number (Optional) OSHH-001/C05US 158166-2025
In re Application of: Youssef BIADILLAH et al. Application No.: 17/510,003 Filed: October 25, 2021 For: BIOLOGICAL COLLECTION SYSTEM The applicant, <u>DNA GENOTEK, INC.</u>, owner of <u>100</u> percent interest in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of prior patent No. <u>11,00,646</u> as the term of said prior patent is presently shortened by any terminal disclaimer. The applicant hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the prior patent are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns. In making the above disclaimer, the applicant does not disclaim the terminal part of the term of any patent granted on the instant application that would extend to the expiration date of the full statutory term of the prior patent, "as the term of said prior patent is presently shortened by any terminal disclaimer," in the event that said prior patent later: - expires for failure to pay a maintenance fee; - is held unenforceable; - is found invalid by a court of competent jurisdiction; - is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321; - has all claims canceled by a reexamination certificate; - is reissued; or - is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer. Check either box 1 or 2 below, if appropriate. 1. ☐ The undersigned is the applicant. If the applicant is an assignee, the undersigned is authorized to act on behalf of the assignee. I hereby acknowledge that any willful false statements made are punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both. 2. ☒ The undersigned is an attorney or agent of record. Reg. No. <u>80,682</u> <u>/Mengran Liu/</u> Signature <u>October 24, 2022</u> Date <u>Mengran Liu</u> Typed or printed name <u>Attorney for Applicant(s)</u> Title <u>(650) 843-5114</u> Telephone Number ☐ Terminal disclaimer fee under 37 CFR 1.20(d) included. WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.	

Application Number * 17/510,003 *	Application/Control No. 17/510,003	Applicant(s)/Patent under Reexamination BIADILLAH et al.	
	Examiner SIEFKE, SAMUEL P	Art Unit 1797	
Document Code - DISQ		Internal Document - DO NOT MAIL	

TERMINAL DISCLAIMER	☐ APPROVED	☒ DISAPPROVED
Date Filed: <u>24 October 2022</u>	This patent is subject to a Terminal Disclaimer	

Approved/Disapproved by:
/FELICIA D ROBERTS/ Technology Center: <u>OPLC</u> Telephone: <u>(571)272-0550</u> <u>The prior patent is incorrect.</u> <u>Please correct and resubmit the TD. (No new fee required)</u>

TERMINAL DISCLAIMER TO OBVIATE A DOUBLE PATENTING REJECTION OVER A "PRIOR" PATENT	Docket Number (Optional) OSHH-001/C05US 158166-2025
--	--

In re Application of: Youssef BIADILLAH et al.

Application No.: 17/510,003

Filed: October 25, 2021

For: BIOLOGICAL COLLECTION SYSTEM

The applicant, DNA GENOTEK, INC., owner of 100 percent interest in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of **prior patent** No. 11,002,646 as the term of said **prior patent** is presently shortened by any terminal disclaimer. The applicant hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the **prior patent** are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

In making the above disclaimer, the applicant does not disclaim the terminal part of the term of any patent granted on the instant application that would extend to the expiration date of the full statutory term of the **prior patent**, "as the term of said **prior patent** is presently shortened by any terminal disclaimer," in the event that said **prior patent** later:

- expires for failure to pay a maintenance fee;
- is held unenforceable;
- is found invalid by a court of competent jurisdiction;
- is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321;
- has all claims canceled by a reexamination certificate;
- is reissued; or
- is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.

Check either box 1 or 2 below, if appropriate.

1. ☐ The undersigned is the applicant. If the applicant is an assignee, the undersigned is authorized to act on behalf of the assignee.

I hereby acknowledge that any willful false statements made are punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

2. ☒ The undersigned is an attorney or agent of record. Reg. No. 80,682

/Mengran Liu/
Signature

Mengran Liu
Typed or printed name

Agent for Applicant
Title

November 1, 2022
Date

(650) 843-5114
Telephone Number

☐ Terminal disclaimer fee under 37 CFR 1.20(d) included.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

Application Number * 17/510,003 *	Application/Control No. 17/510,003	Applicant(s)/Patent under Reexamination BIADILLAH et al.	
	Examiner SIEFKE, SAMUEL P	Art Unit 1797	
Document Code - DISQ		Internal Document - DO NOT MAIL	

TERMINAL DISCLAIMER	☒ APPROVED	☐ DISAPPROVED
Date Filed: <u>01 November 2022</u>	This patent is subject to a Terminal Disclaimer	

Approved/Disapproved by:
/JEAN PROCTOR/ Technology Center: <u>OPLC</u> Telephone: <u>(571)272-1040</u> _____

PART B-FEE(S) TRANSMITTAL

Complete and send this form, together with the applicable fee(s), by mail or fax, or via EFS-Web.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

By fax, send to: (571) 273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

COOLEY LLP
ATTN: Patent Group
1299 Pennsylvania Avenue, NW
Suite 700
Washington, DC 20004

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via EFS-Web or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
17/510,003	10/25/2021	Youssef BIADILLAH	OSHH-001/C05US 158166-2025	3950

TITLE OF INVENTION: BIOLOGICAL COLLECTION SYSTEM

APPLN: TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1,200.00			\$1,200.00	12/07/2022

EXAMINER	ART UNIT	CLASS-SUBCLASS
S. P. Siefke	1797	

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363)

- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-09 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

- (1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1. COOLEY LLP

2.

3.

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE or COUNTRY)

DNA GENOTEK, INC.

Ottawa, Canada

Please check the appropriate assignee category or categories (will not be printed on the patent):

☐ Individual ☒ Corporation or other private group entity ☐ Government4a. Fees Submitted: ☒ Issue Fee ☐ Publication Fee (if required) ☐ Advance Order - # of Copies _____

4b. Method of Payment (Please first reapply any previously paid fee shown above):

☒ Electronic Payment via EFS-Web ☐ Enclosed check ☐ Non-electronic payment by credit card (Attach form PTO-2038)☒ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. 50-1283

5. Change of Entity Status (from status indicated above)

- ☐ Applicant certifying micro entity status. See 37 CFR 1.29.
☐ Applicant asserting small entity status. See 37 CFR 1.27.
☐ Applicant changing to regular undiscounted fee status.

NOTE: Absent a valid Certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

NOTE: If the application was previously under micro entity status, checking this box will be taken as a notification of loss of entitlement to micro entity status.

NOTE: Checking this box will be taken as a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature

/Mengran Liu/

Date November 18, 2022

Typed or printed name

Mengran Liu

Registration No. 80,682



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/510,003	12/27/2022	11536632	OSHH-001C05US 158166-2025	3950

58249 7590 12/07/2022
COOLEY LLP
ATTN: IP Docketing Department
1299 Pennsylvania Avenue, NW
Suite 700
Washington, DC 20004

ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment is 0 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Patents Stakeholder Experience (OPSE), Stakeholder Support Division (SSD) at (571)-272-4200.

INVENTOR(s) (Please see PAIR WEB site <http://pair.uspto.gov> for additional inventors):

Youssef BIADILLAH, Geneva, SWITZERLAND;
Stephen D. ANDREWS, Falmouth, ME;

APPLICANT(s) (Please see PAIR WEB site <http://pair.uspto.gov> for additional applicants):

DNA GENOTEK, INC., Ottawa, CANADA;

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