

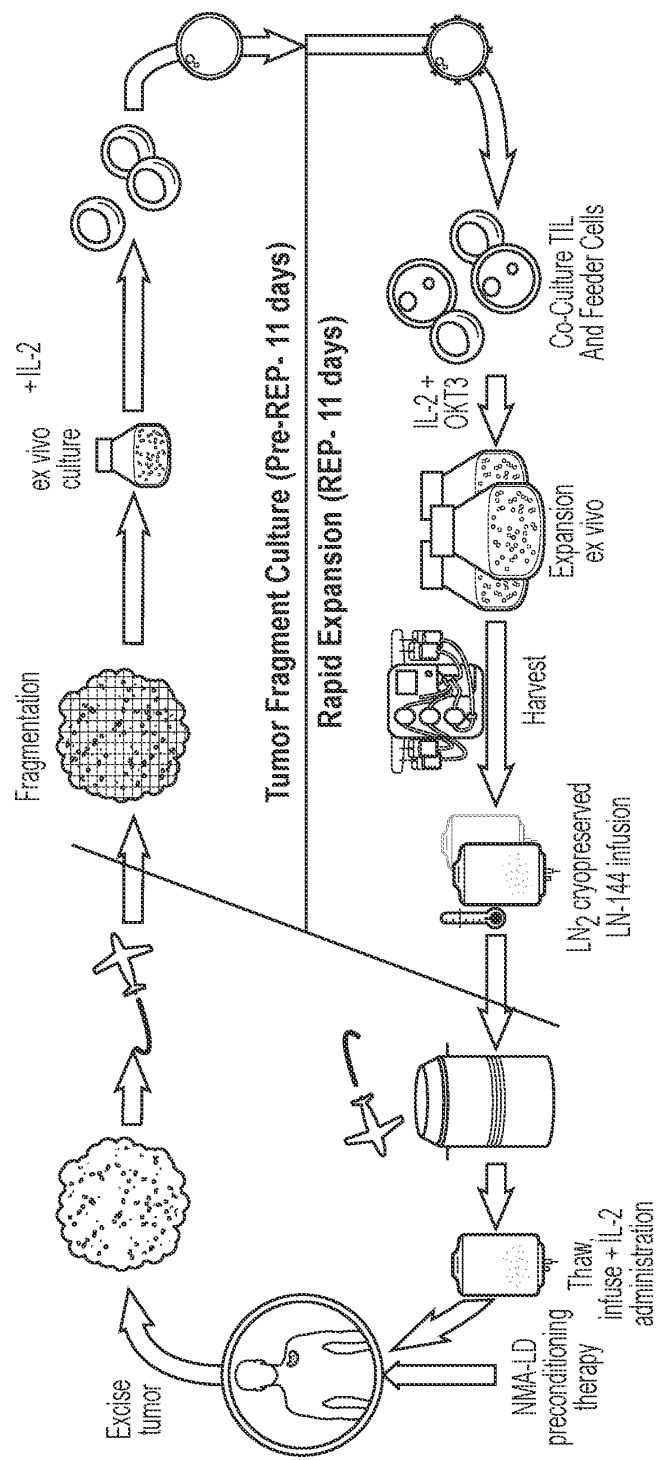


FIG. 1

2/29

Process GEN 3: about 14-18 days from Steps A - E**STEP A**

Obtain Patient Tumor Sample
(optionally can be frozen before Step B)

STEP B

Priming First Expansion
(physical fragmentation of up to 60 fragments per container grown for about 1 days to 7/8 days with media comprising IL-2, OKT-3, and optionally antigen-presenting feeder cells)

STEP C

Priming First Expansion to Rapid Second Expansion Transition
(Step B TILs directly move to Step D on day 7/8)

STEP D

Rapid Second Expansion
(TILs grown in growth media medium comprising IL-2, OKT-3, and 2X antigen-presenting feeder cells; Days 10-11 scale up and add additional IL-2)

STEP E

Harvest TILS from Step D

STEP F

Final Formulation and/or Transfer to Infusion Bag
(optionally cryopreserve)

FIG. 2A

3/29

Process 2A: about 22 days from Steps A - E	Process GEN 3: about 14-18 days from Steps A - E
<u>STEP A</u> Obtain Patient Tumor Sample (optionally can be frozen before Step B; optionally tumor sample can be a core/small biopsy)	<u>STEP A</u> Obtain Patient Tumor Sample (optionally can be frozen before Step B)
<u>STEP B</u> First Expansion (physical fragmentation to at least 40 fragments per container grown for about 3 days to 14 days with media comprising IL-2)	<u>STEP B</u> Priming First Expansion (physical fragmentation of up to 60 fragments per container grown for about 1 days to 7/8 days with media comprising IL-2, OKT-3, and optionally antigen-presenting feeder cells)
<u>STEP C</u> First Expansion to Second Expansion Transition (Step B TILs directly move to Step D, optionally on Step B day 11)	<u>STEP C</u> Priming First Expansion to Rapid Second Expansion Transition (Step B TILs directly move to Step D on day 7/8)
<u>STEP D</u> Second Expansion (TILs grown in growth media medium comprising IL-2, OKT-3, and antigen-presenting feeder cells in a closed container)	<u>STEP D</u> Rapid Second Expansion (TILs grown in growth media medium comprising IL-2, OKT-3, and 2X antigen-presenting feeder cells; Days 10-11 scale up and add additional IL-2)
<u>STEP E</u> Harvest TILS from Step D (TILs harvested via closed system)	<u>STEP E</u> Harvest TILS from Step D
<u>STEP F</u> Final Formulation and/or Transfer to Infusion Bag (optionally cryopreserve)	<u>STEP F</u> Final Formulation and/or Transfer to Infusion Bag (optionally cryopreserve)

FIG. 2B

4/29

Embodiment GEN 3.0: about 14-18 days from Steps A - E	Embodiment GEN 3.1 control: about 14-18 days from Steps A - E	Embodiment GEN 3.1 Test/F: about 14-18 days from Steps A - E
STEP A Obtain Patient Tumor Sample (optionally can be frozen before Step B)	STEP A Obtain Patient Tumor Sample (optionally can be frozen before Step B)	STEP A Obtain Patient Tumor Sample (optionally can be frozen before Step B)
STEP B Priming First Expansion (physical fragmentation of up to 60 fragments per container grown for about 1 days to 7/8 days with media comprising IL-2)	STEP B Priming First Expansion (physical fragmentation of up to 60 fragments per container grown for about 1 days to 7/8 days with media comprising IL-2, and OKT-3)	STEP B Priming First Expansion (physical fragmentation of up to 60 fragments per container grown for about 1 days to 7/8 days with media comprising IL-2, OKT-3, and antigen- presenting feeder cells)
STEP C Priming First Expansion to Rapid Second Expansion Transition (Step B TILs directly move to Step D on day 7/8)	STEP C Priming First Expansion to Rapid Second Expansion Transition (Step B TILs directly move to Step D on day 7/8)	STEP C Priming First Expansion to Rapid Second Expansion Transition (Step B TILs directly move to Step D on day 7/8)
STEP D Rapid Second Expansion (TILs grown in growth media medium comprising IL-2, OKT-3, and antigen-presenting feeder cells; Days 10-11 scale up and add additional IL-2)	STEP D Rapid Second Expansion (TILs grown in growth media medium comprising IL-2, OKT-3, and 2X antigen- presenting feeder cells; Days 10-11 scale up and add additional IL-2)	STEP D Rapid Second Expansion (TILs grown in growth media medium comprising IL-2, OKT-3, and 2X antigen- presenting feeder cells; Days 10-11 scale up and add additional IL-2)
STEP E Harvest TILS from Step D	STEP E Harvest TILS from Step D	STEP E Harvest TILS from Step D
STEP F Final Formulation and/or Transfer to Infusion Bag (optionally cryopreserve)	STEP F Final Formulation and/or Transfer to Infusion Bag (optionally cryopreserve)	STEP F Final Formulation and/or Transfer to Infusion Bag (optionally cryopreserve)

FIG. 2C

5/29

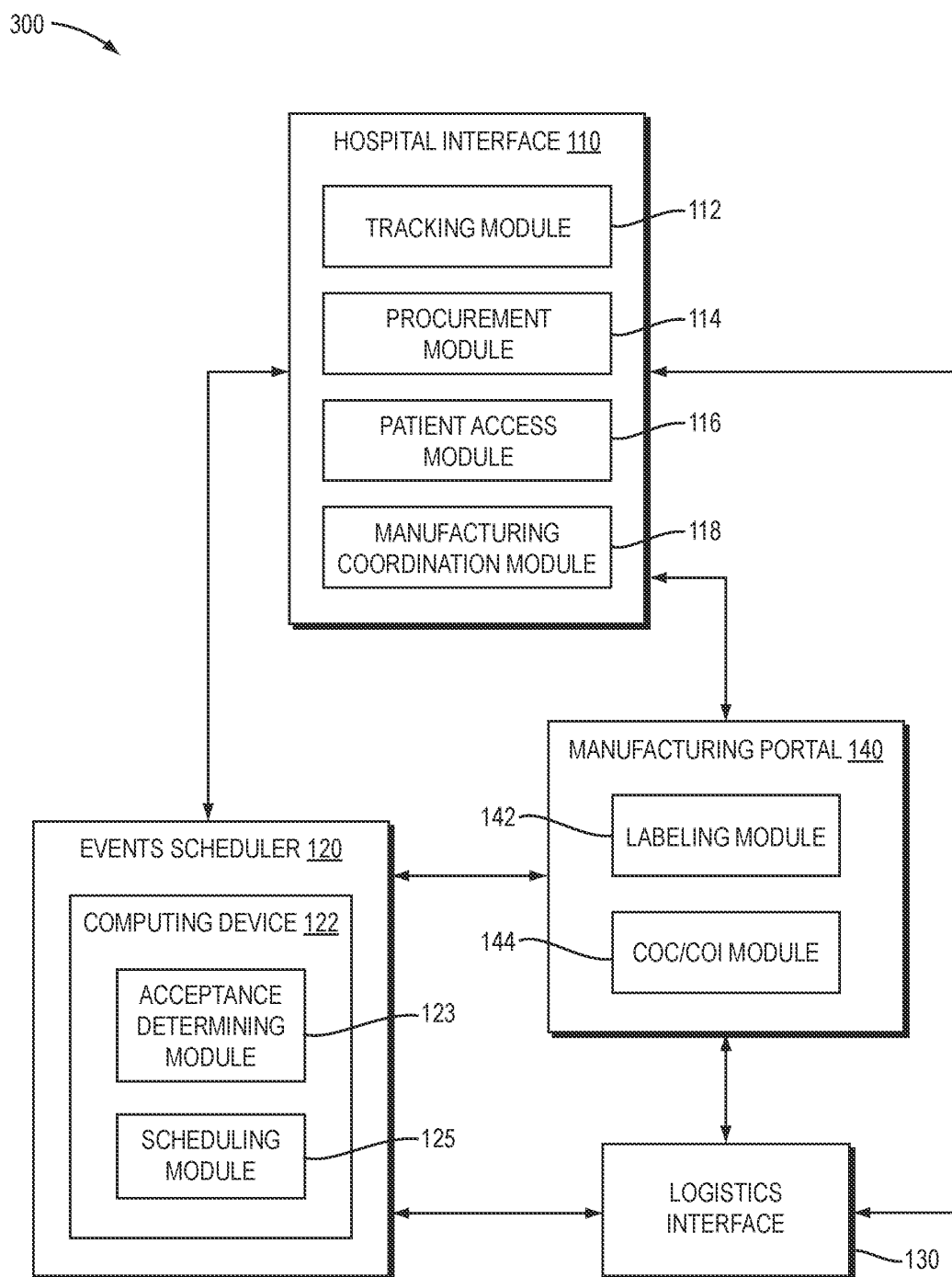


FIG. 3A

6/29

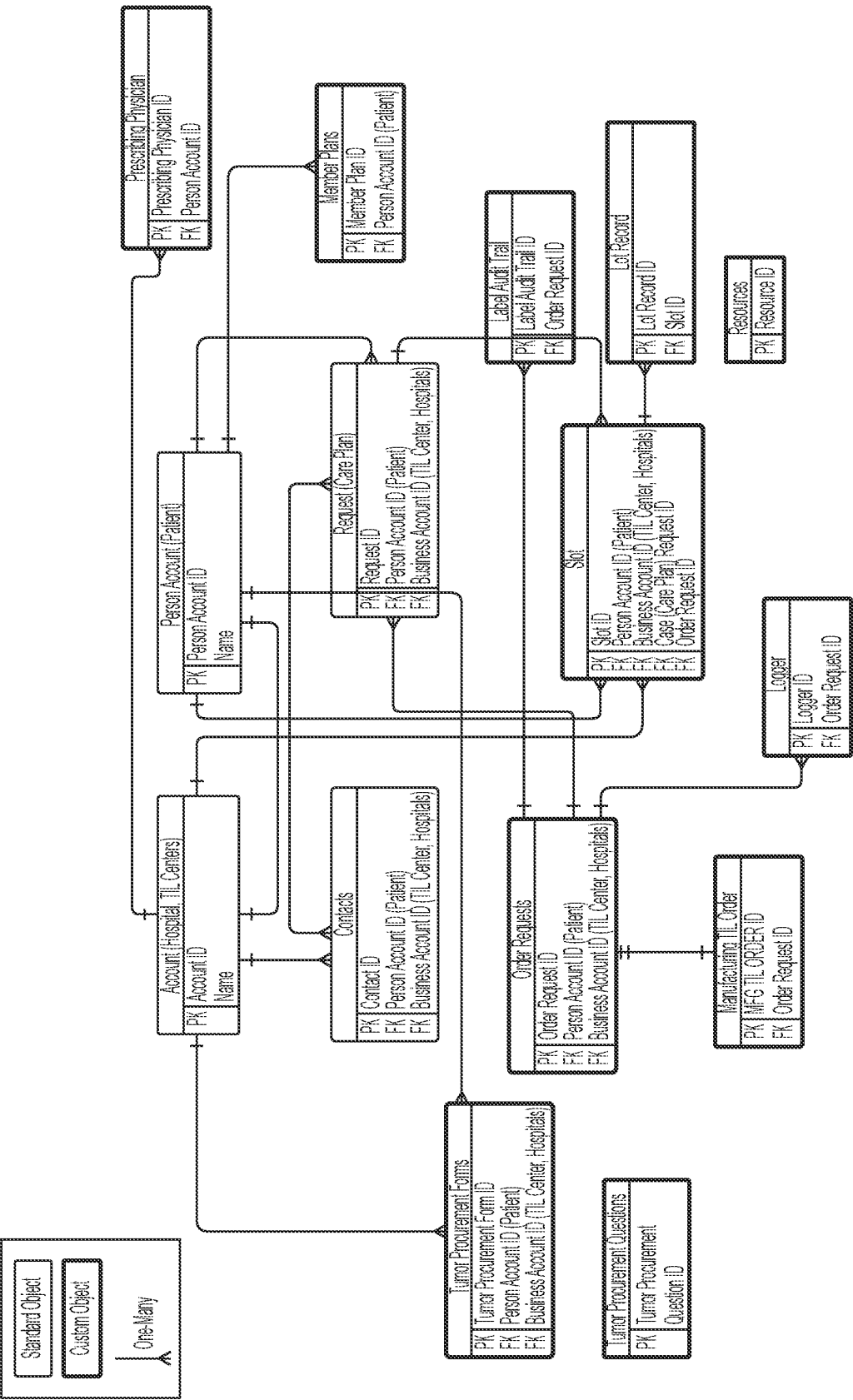


FIG. 3B

7/29

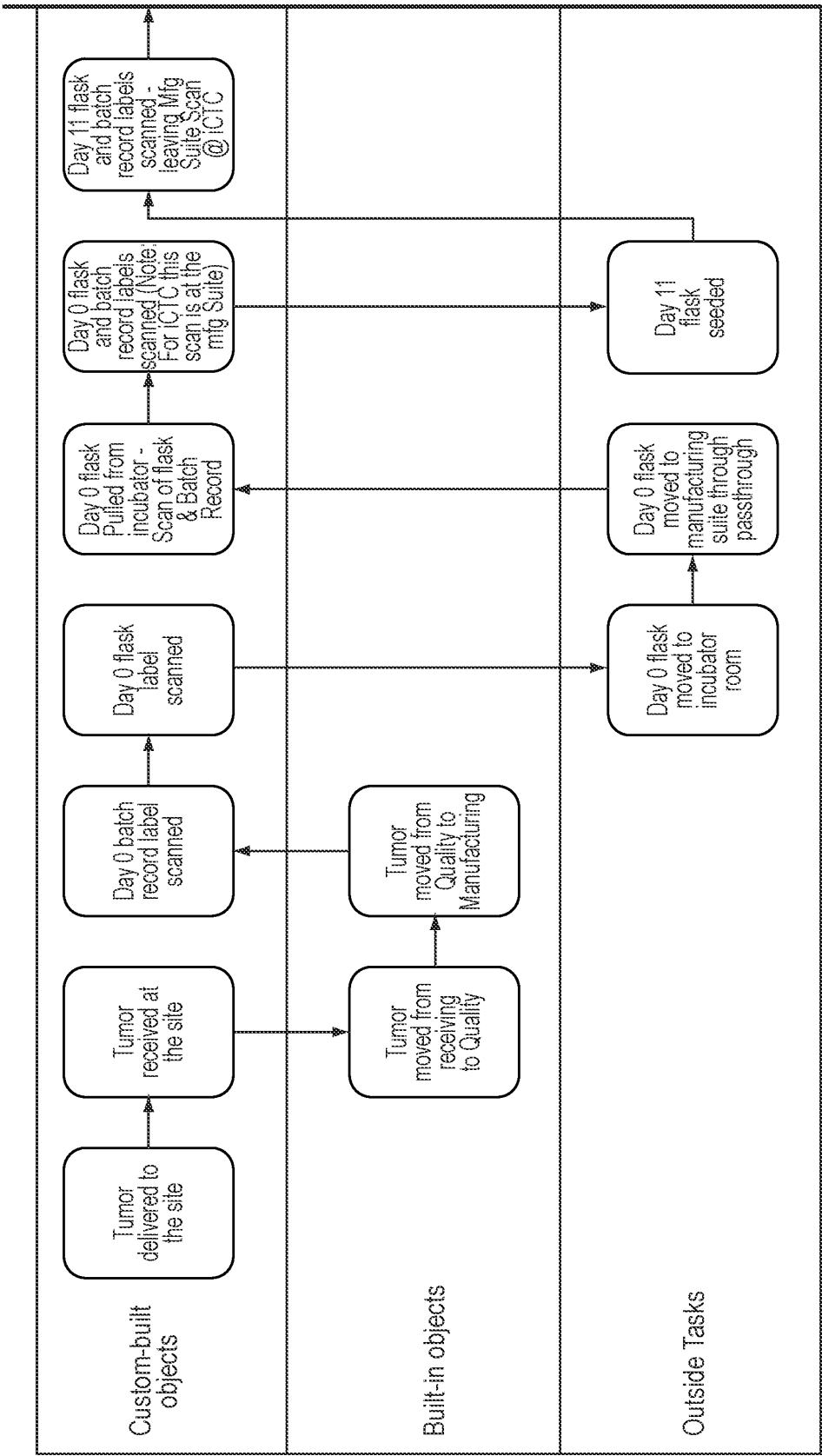


FIG. 3C

To FIG. 3D

8/29

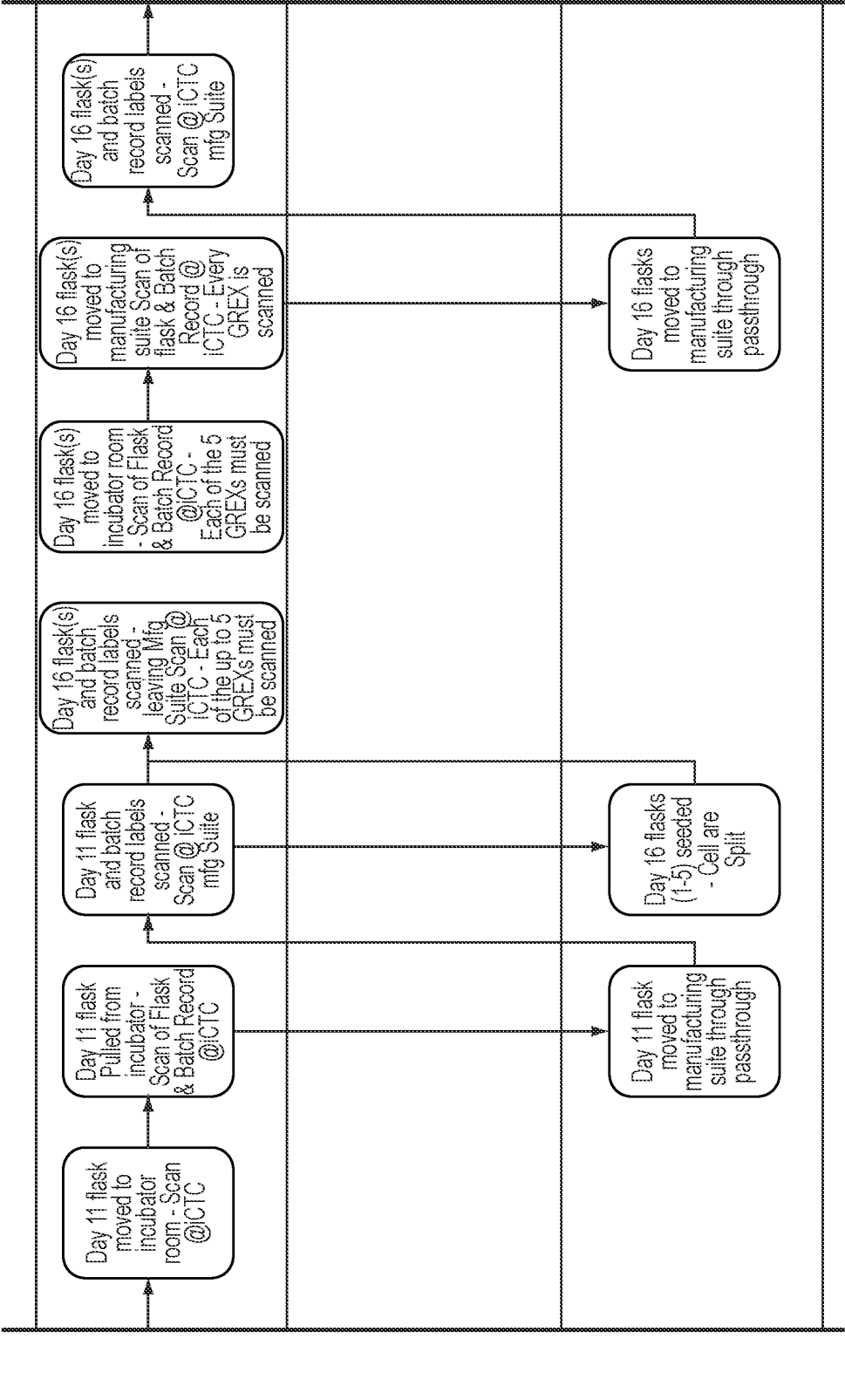
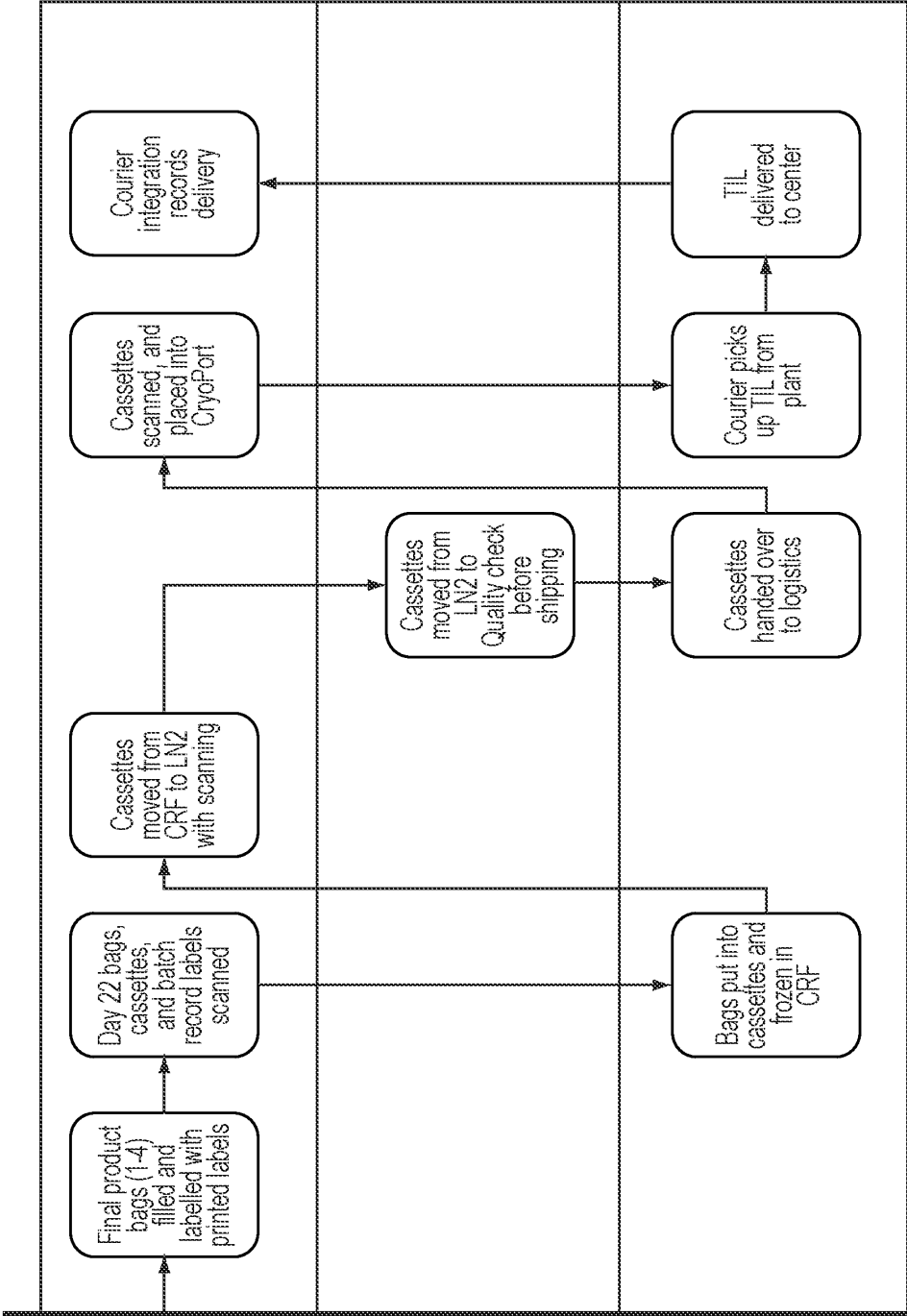


FIG. 3D

To FIG. 3E

From FIG. 3C

9/29



From FIG. 3D

FIG. 3E

10/29

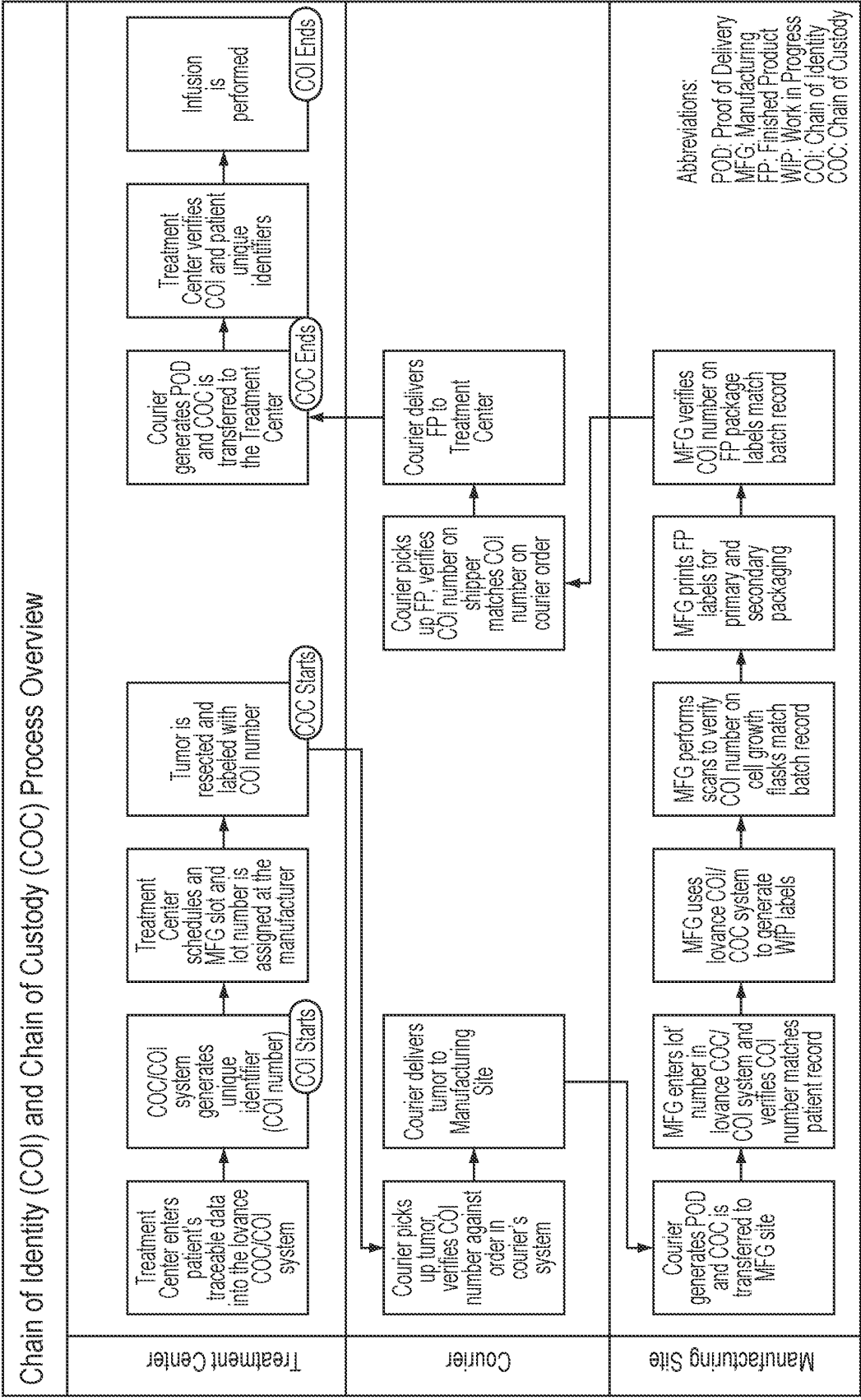


FIG. 3F

11/29

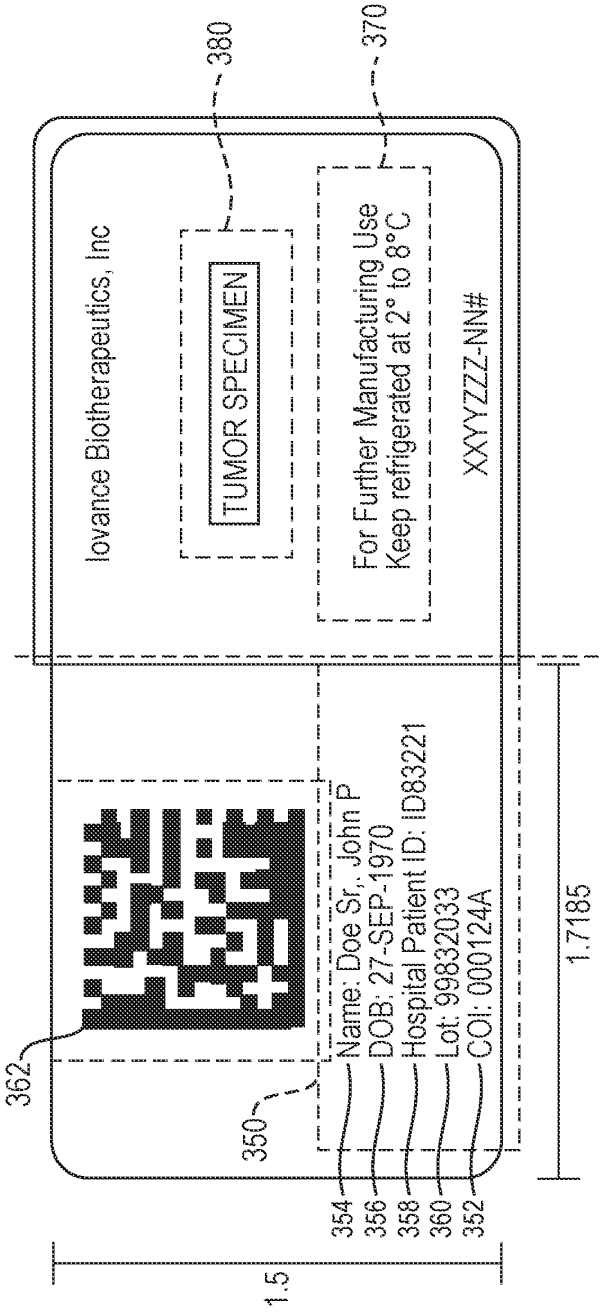
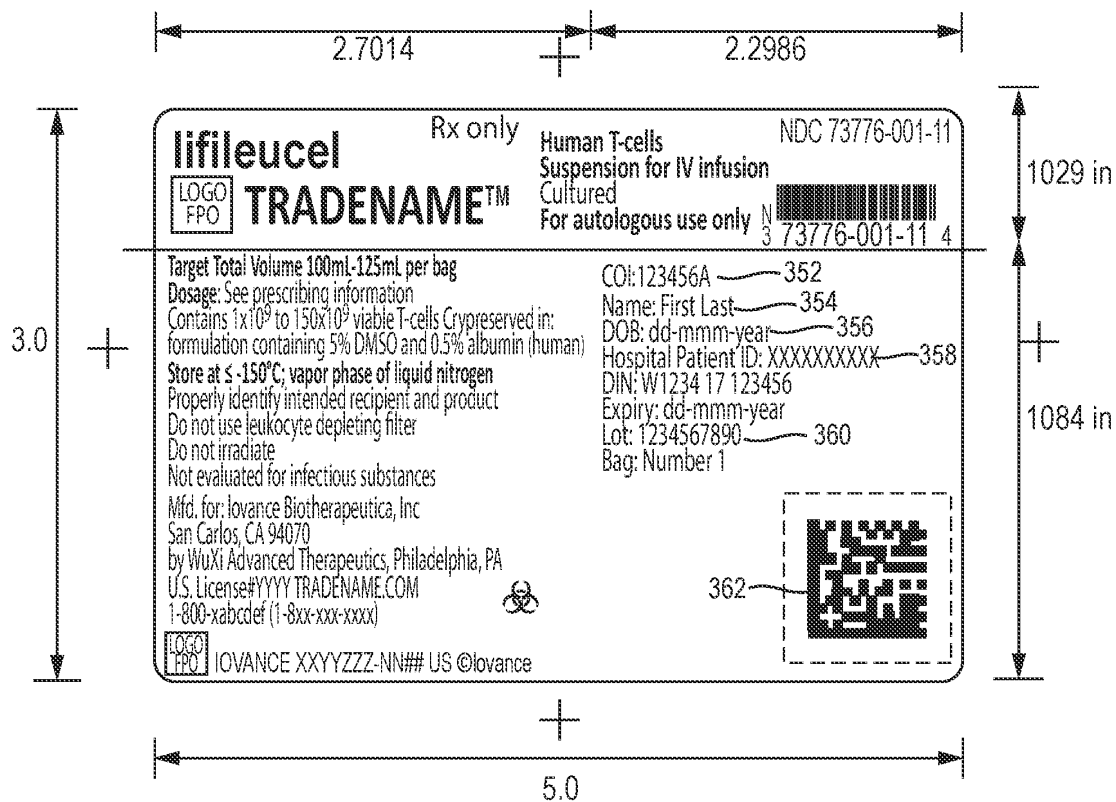
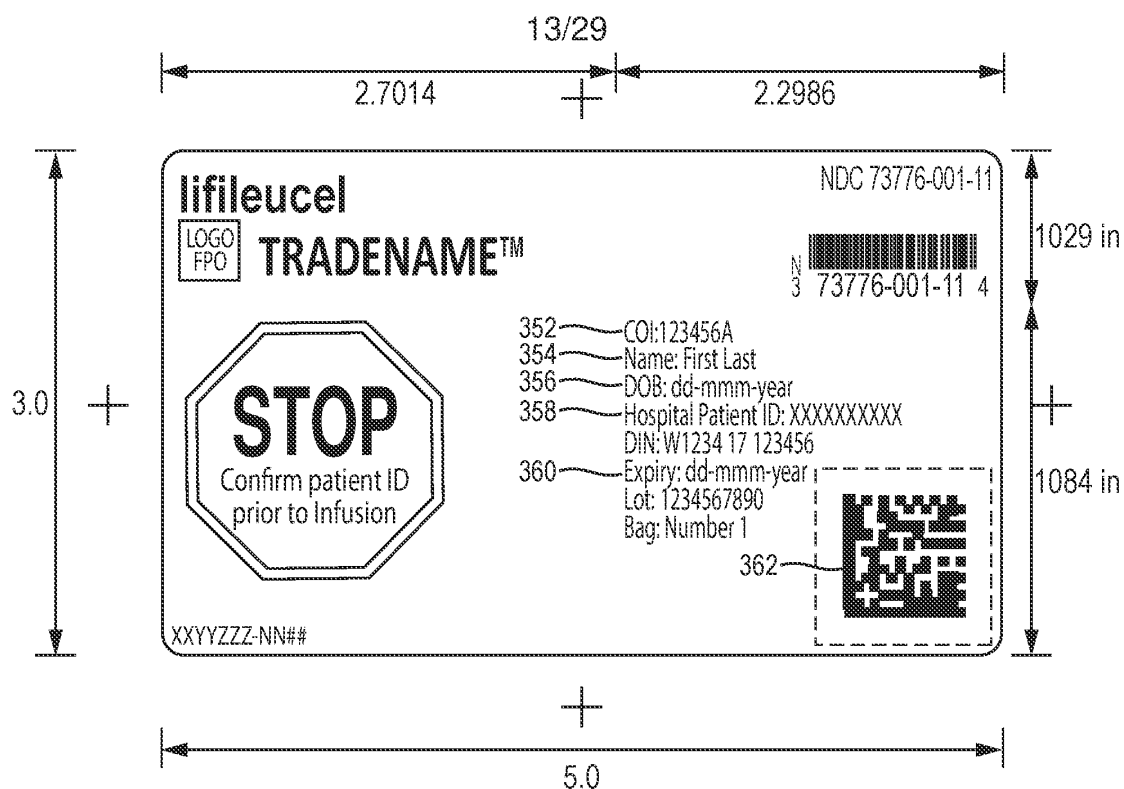


FIG. 3G

12/29

#	Label Type & Barcode Type	Quantity	Description
1	Tumor Shipper	1	Label needed to ship raw materials from the center to plant
2	Tumor Media Bottle	1	Label for the bottle that the raw material will be placed in for storage during the shipment to plant
3	In Process	11	Labels needed for Day 0, Day 11, and Day 16 Flasks and Batch Record
4	Day 22 - Bag 1	2	Labels needed for Final Product Bag 1 and Cassette 1
5	Day 22 - Bag 2	2	Labels needed for Final Product Bag 2 and Cassette 2
6	Day 22 - Bag 3	2	Labels needed for Final Product Bag 3 and Cassette 3
7	Day 22 - Bag 4	2	Labels needed for Final Product Bag 4 and Cassette 4
8	Day 22 - Batch	1	Label needed for Day 22 Batch Record
9	TIL Shipper	1	Label needed to ship final product from plant to the center

FIG. 3H



14/29

Home	Tumor Procurement Module	Resources
	Print TPF	Transfer Ownership Remove Ownership
Details		
General		
TPF Owner	Leonard Brown	
TPF Status	Complete	
Hospital Patient ID	CPMC-STP-01	
Patient Name	Spags T Patient 01	
Date Of Birth	01/01/1990	
COI Number	202101002A	
Lot Number	STP-LOT-01	
TIL Center Name	California Pacific Medical Center	
Indication	Metastatic Melanoma	
Resection Date	04/07/2021	
Notes		
Screen 1 Check Materials		
Sterile Transfer Pipettes, Quantity = 4	☐	
Parafilm, Quantity = 6	☐	
Transport Bags w/Absorbent Sheets, Quantity = 1	☐	
Label Sheet with Tumor Bottle Label and Shipper Box Label	☐	
Specimen Washing Containers, Quantity = 4, Serial # / Lot #	Done	
Specimen Washing Containers - Expiration Date	04/30/2021	
Temperature Monitor, Quantity = 1, Serial # / Lot #	Done	
Temperature Monitor - Expiration Date	04/30/2021	

FIG. 3K

16/29

Specimen Washing Containers - Expiration Date	04/30/2021
Temperature Monitor, Quantity = 1, Serial # / Lot #	Done
Temperature Monitor - Expiration Date	04/30/2021
NanoCool, Quantity = 1 - Serial # / Lot #	Done
NanoCool - Expiration Date	04/30/2021
HBSS, Quantity = 1 - Serial # / Lot #	Done
HBSS - Expiration Date	04/30/2021
Gentamicin, Quantity = 1 - Serial # / Lot #	Done
Gentamicin - Expiration Date	04/30/2021
Amphotericin B, Quantity = 1 - Serial # / Lot #	Done
Amphotericin B - Expiration Date	04/30/2021
HypoThermosol, Quantity = 1 - Serial # / Lot #	Done
HypoThermosol - Expiration Date	04/30/2021
~ Screen 1 Prepare Materials	
The Amphotericin B bottle has been removed from the freezer and defrosted.	☒
The Gentamicin bottle has been removed from the refrigerator.	☒
The amount of 0.5 mL of Amphotericin B and 0.5 mL of Gentamicin have been added to the HypoThermosol bottle. The remaining Amphotericin B and Gentamicin provided by Iovance should be discarded.	☒
Iovance provided label has been verified and applied to the HypoThermosol bottle. Verify patient details against hospital records. Specimen bottle labels: Patient ID, COI #, DOB	☒
~ Screen 1 Approval	
Screen 1 Confirmation	☒
Screen 1 Confirmed By	Leonard Brown
Screen 1 Verification	☒

FIG. 3M

17/29

Screen 1 Confirmation	☒
✓ Screen 1 Confirmed By	Leonard Brown
Screen 1 Verification	☒
Screen 1 Verified By	Cal Pacific TPV
Screen 2 Tumor Procurement Details	
Media transported to OR by	Done
Media received in OR by	Done
Name of Surgeon performing Tumor Procurement	Done
Time first Tumor procured (24 hr-hhmm)	04/07/2021 03:00
Time last Tumor procured (24 hr-hhmm)	04/07/2021 03:00
# of lesions procured	1
Location(s) of lesions procured	
LOCATION NAME	
Done	
Has the ideal amount of viable tumor of at least 1.5 cm, but no more than 4.0 cm in diameter (aggregate) for TIL isolation/manufacturing been obtained?	Yes
Was an intraoperative frozen section or biopsy of tumor taken to confirm presence of malignant cells?	Yes
Ensure that the tumor has been washed 3 times in HBSS	☒
✓ Confirm that the Hospital Patient ID and COI match with the labels and Tumor Tissue Procurement Form	☒
Time Last Tumor is placed in HypoThermosol (24 hr-hhmm)	04/07/2021 03:00
Screen 2 Tumor Containment Details	
Ensure the tumor is placed in the 100 mL specimen bottle containing the HypoThermosol/Gentamicin/Amphotericin B solution (at 2-8 C) with the lid tightly closed and wrapped in parafilm	☒
Ensure the pre-printed tumor specimen label has been affixed to the	☒

FIG. 3N

18/29

Ensure the tumor is placed in the 100 mL specimen bottle containing the HypoThermosol/Gentamicin/Amphotericin B solution (at 2-8 C) with the lid tightly closed and wrapped in parafilm	☒
Ensure the pre-printed tumor specimen label has been affixed to the specimen bottle with the required and verified information	☒
Ensure the specimen bottle has been placed in the transport bag with absorbent pads and sealed	☒
If available, document the DIN (Donation Identification Number):	N/A
~ Screen 2 Approval	
Screen 2 Confirmation	☒
Screen 2 Confirmed By	Leonard Brown
Screen 2 Verification	☒
Screen 2 Verified By	Cal Pacific TPV
~ Screen 3 Tumor Packout Details	
Ensure the 2 Cooling Engines in the NanoCool been activated (Represented by the Light Blue "NanoCool" Logo) - Typically takes 5 minutes to fully activate	☒
Verify the temperature monitor matches with the serial # and expiry captured in section 1 of this form	☒
Ensure the temperature monitor has been activated and affix the temperature monitor to the transport bag containing the tumor specimen	☒
Ensure the transport bag containing the specimen bottle is placed in the NanoCool	☒
Ensure to check and affix the shipper box labels from the printed label sheet to the outer side of the NanoCool	☒
Ensure the Correct Courier Bill of Lading (BOL) has been securely affixed to the outside of the NanoCool. Note: The Correct BOL utilizes a reference number that will match the COI number of the Patient Specimen and COI Number captured on this form.	☒
Ensure the NanoCool has been sealed with tamper evident tape	☒

FIG. 30

19/29

Screen 3 Tumor Packout Details	
Ensure the 2 Cooling Engines in the NanoCool been activated (Represented by the Light Blue "NanoCool" Logo) - Typically takes 5 minutes to fully activate	☒
Verify the temperature monitor matches with the serial # and expiry captured in section 1 of this form	☒
Ensure the temperature monitor has been activated and affix the temperature monitor to the transport bag containing the tumor specimen	☒
Ensure the transport bag containing the specimen bottle is placed in the NanoCool	☒
Ensure to check and affix the shipper box labels from the printed label sheet to the outer side of the NanoCool	☒
Ensure the Correct Courier Bill of Lading (BOL) has been securely affixed to the outside of the NanoCool. Note: The Correct BOL utilizes a reference number that will match the COI number of the Patient Specimen and COI Number captured on this form.	☒
Ensure the NanoCool has been sealed with tamper evident tape	☒
Time NanoCool Packing was completed (24 hr-hhmm)	04/07/2021 00:00
Screen 3 Approval	
Screen 3 Confirmation	☒
Screen 3 Confirmed By	Leonard Brown
Screen 3 Verification	☒
Screen 3 Verified By	Cal Pacific TPV
TPF Files	
Upload Scanned TPF	
Upload Files Or drop files	

FIG. 3P

20/29

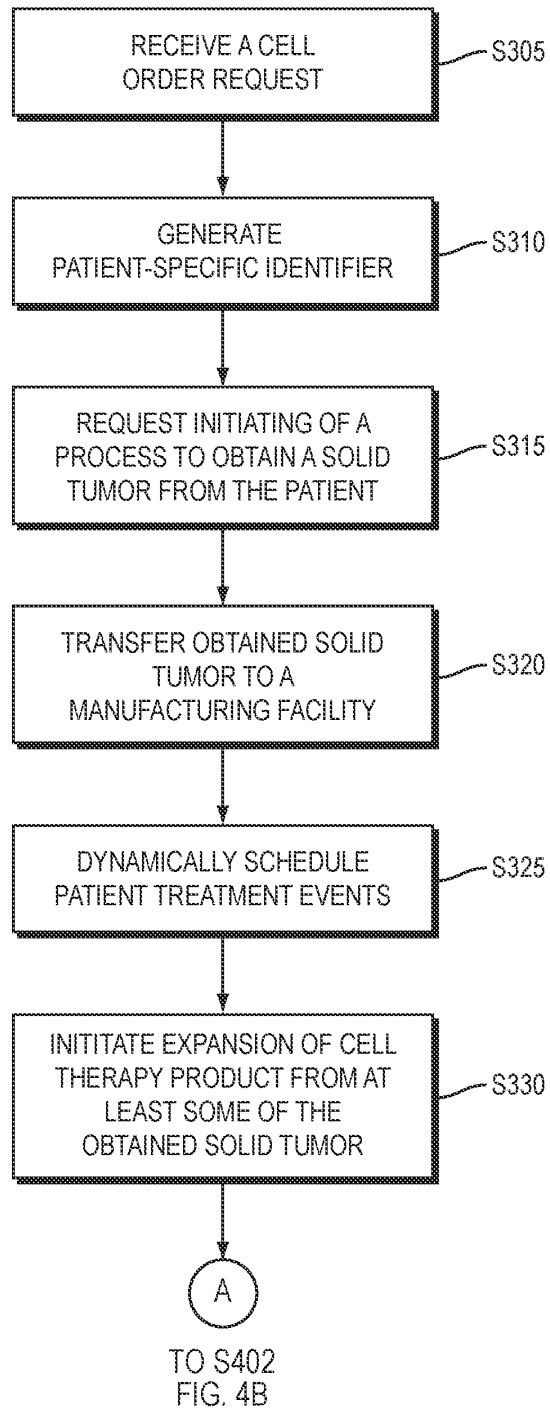
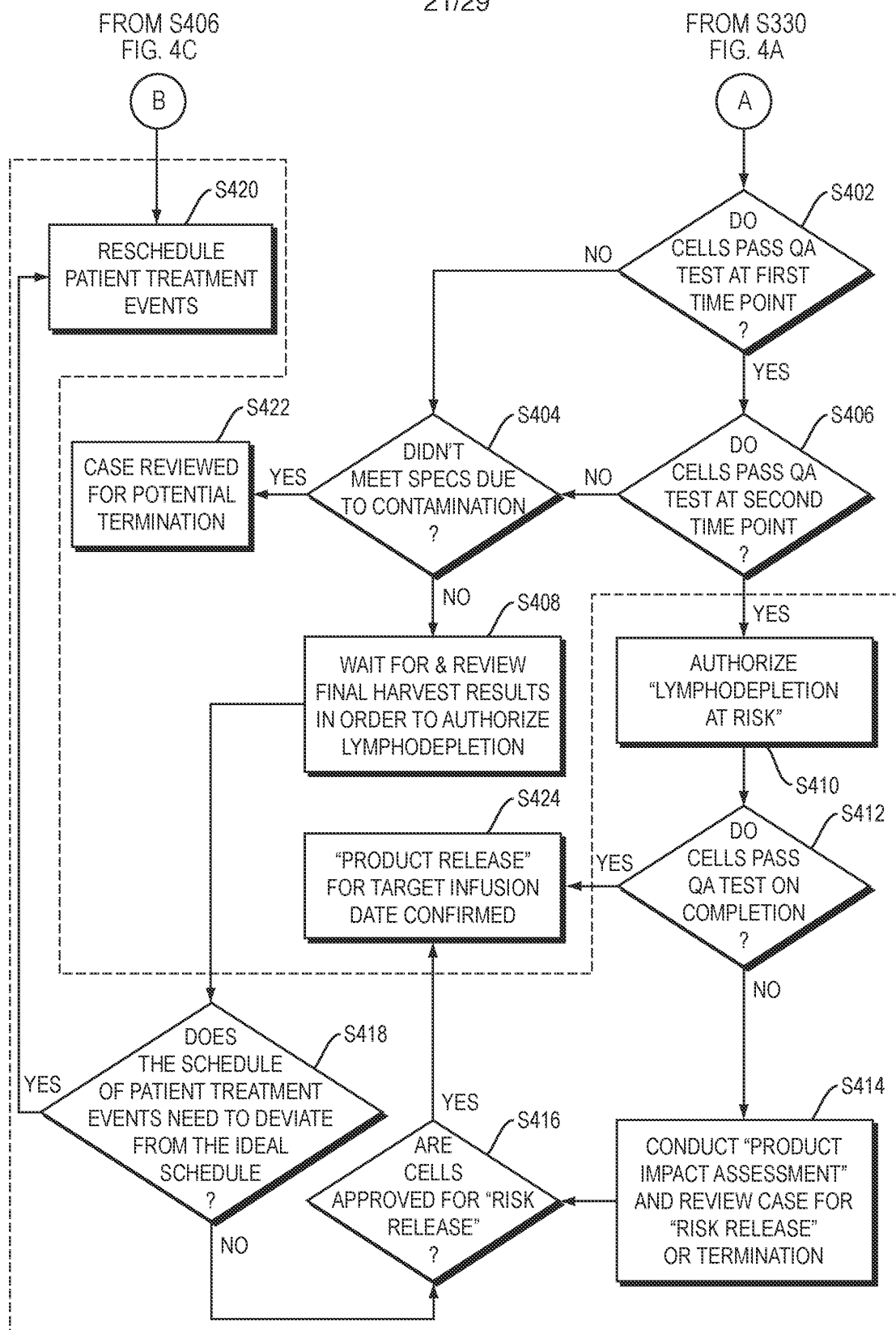


FIG. 4A

21/29



22/29

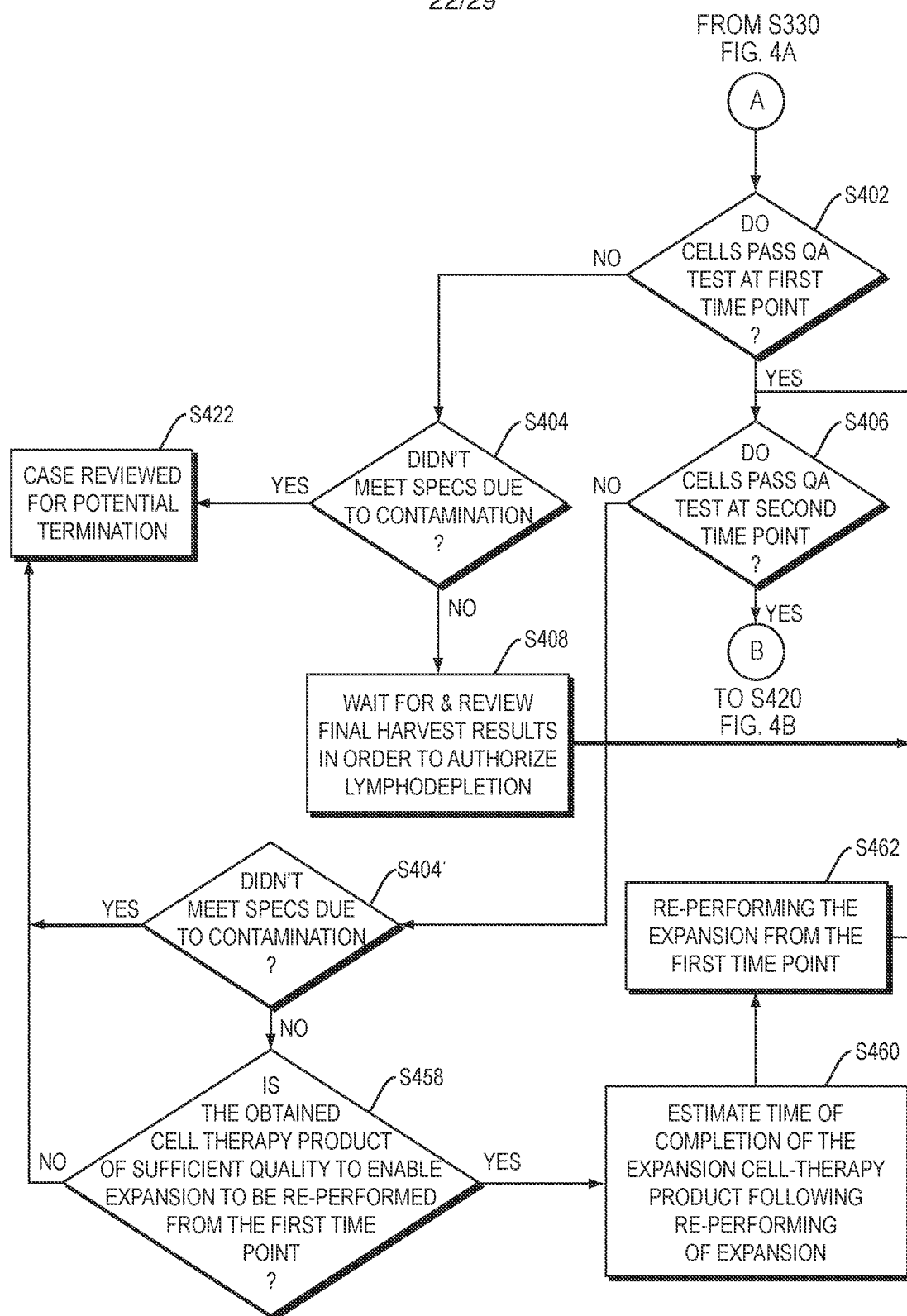


FIG. 4C

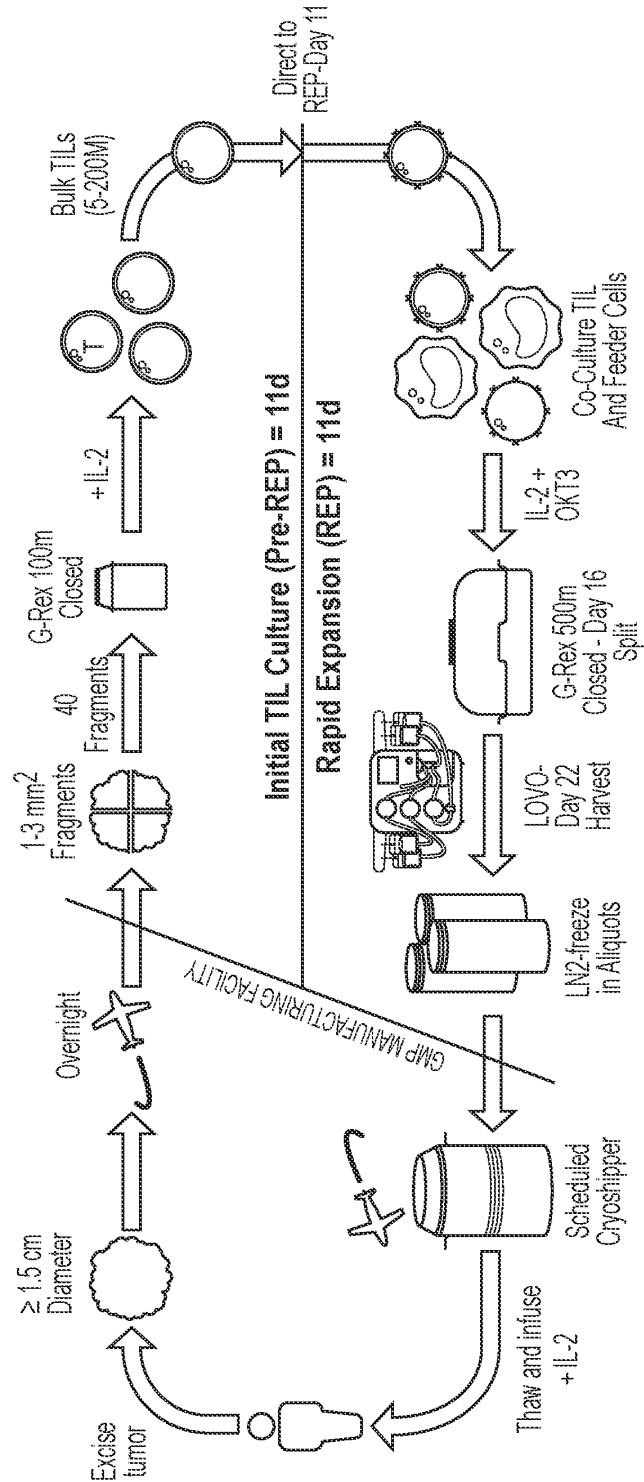


FIG. 5

24/29

Process Development

Step	Process-1C	Process-2A	Impact
1	4 Fragments/10 G-Rex 10-21 Days	40 Fragments/1- G-Rex 100 CS- (x2?) 11 Days	Increases Tumor Sample/Container, Shortens Culture, Reduces Steps, Amenable To Closed System
2	PreREP Freeze-> Testing -> Thaw- ~Day 27- >40e6TIL	Direct To REP- Day 11- <200e6	Shorten Process, Reduces Steps, Eliminates Testing
3	36 G-Rex 100-~Day 30 >5e6TIL - Split ~Day 36	4-5 G-Rex 500CS-TIL- Split Day 16	Reduces Steps, Closed System, Shorter REP
4	Harvest Day ~43+ Harvesting By Centrifugation	Harvest Day 22 LOVO-Automated Cell Washer	Reduces Steps, Automated Closed System
5	Fresh Product- Hypothermosol-Single Infusion Bag	Cryopreserved Product-CS10 In LN ₂ , Multiple Aliquots	Shipping Flexibility, Patient Scheduling, Easier Release Testing, Global Trials
6	43+ Day Process Time	22 Day Process Time	Turnaround To Patient, Clean Room Throughput, COGs

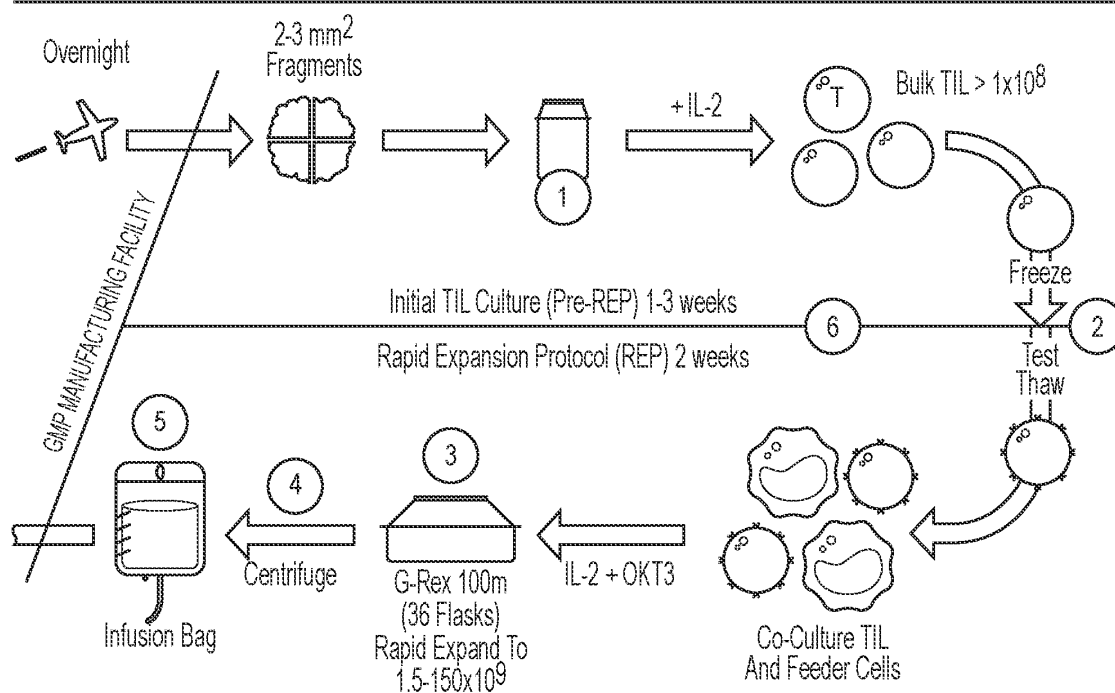


FIG. 6

Timeline - Process 1C

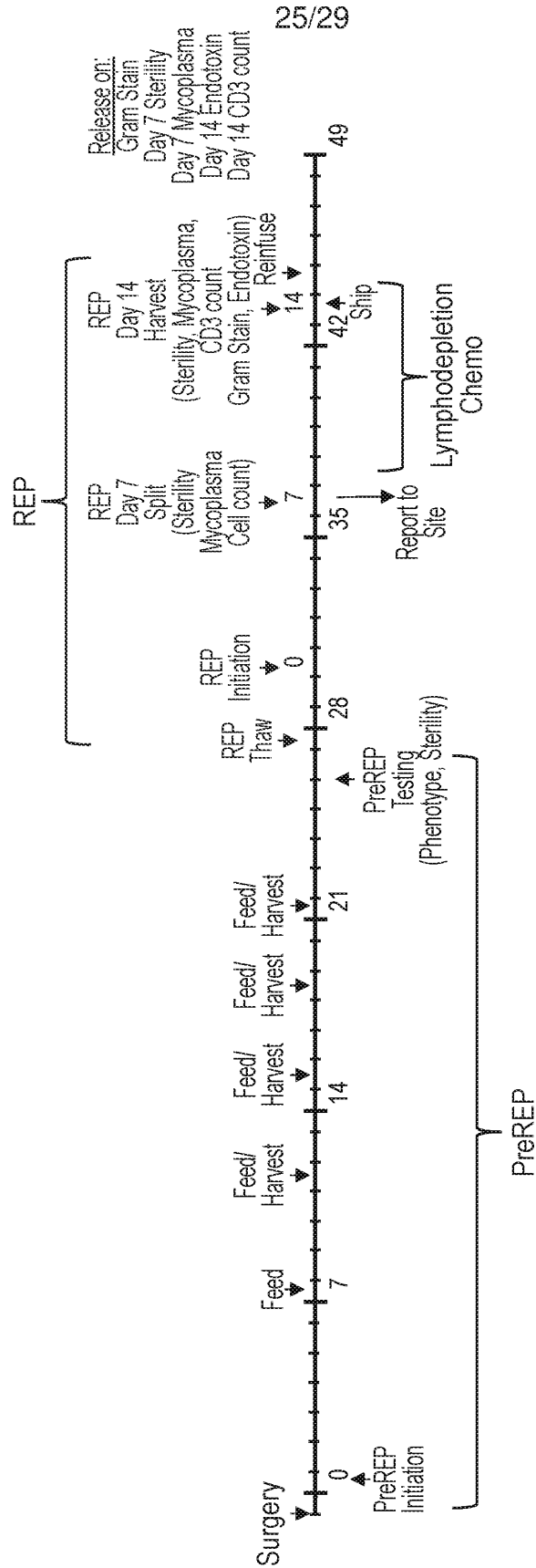


FIG. 7

26/29

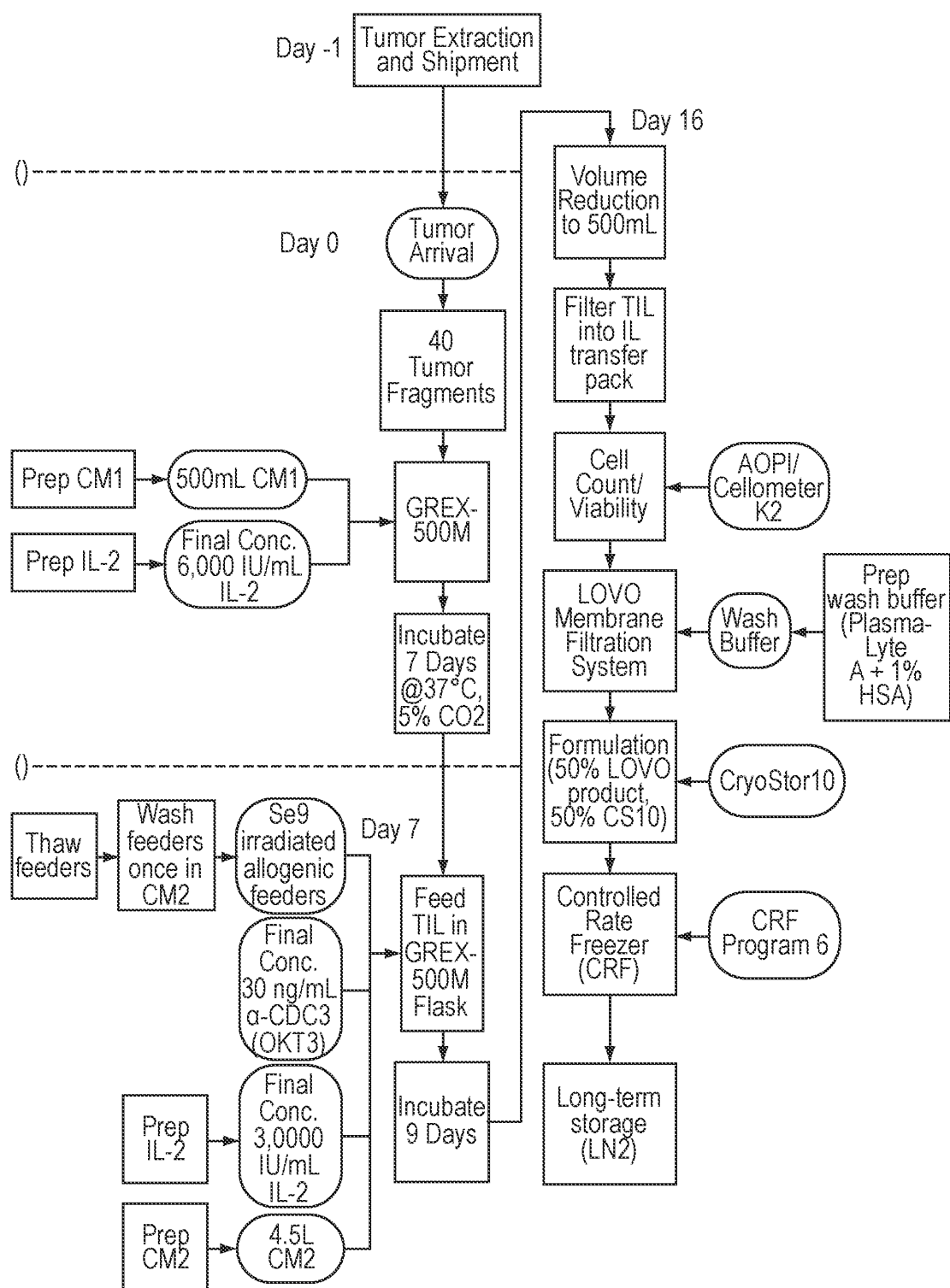


FIG. 8

27/29

Process 2A: about 22 days from Steps A - E

1. STEP A

Obtain Patient Tumor Sample

2. STEP B

Fragmentation and First Expansion

3 days to 14 days

3. STEP C

First Expansion to Second Expansion Transition

No Storage and Closed System

4. STEP D

Second Expansion

IL-2, OKT-3, and antigen-presenting feeder cells

Closed System

5. STEP E

Harvest TILS from Step D

Closed System

6. STEP F

Final Formulation and/or Transfer to Infusion Bag

(optionally cryopreserve)

FIG. 9

28/29

Process 1C: 43 - 55 Days for Steps A - E	Process 2A: About 22 Days from Steps A - E
1. Step A Obtain Patient Tumor Sample	1. Step A Obtain Patient Tumor Sample
2. Step B Fragmentation and First Expansion 11 days to 21 days	2. Step B Fragmentation and First Expansion 3 days to 14 days
3. Step C First Expansion to Second Expansion Transition Optional Storage until Selection	3. Step C First Expansion to Second Expansion Transition No Storage and Closed System
4. Step D Second Expansion IL-2, OKT-3, antigen-presenting feeder cells Optionally repeat one or more times	4. Step D Second Expansion IL-2, OKT-3, antigen-presenting feeder cells Closed System
5. Step E Harvest TILS from Step D	5. Step E Harvest TILS from Step D Closed System
6. Step F Final Formulation and/or Transfer to Infusion Bag	6. Step F Final Formulation and/or Transfer to Infusion Bag (optional cryopreserve)

FIG. 10

29/29

Process Step	Process 1C Embodiment	Process 2A Embodiment	Advantages
Pre-REP	4 fragments per 10 GREX-10 flasks 11-21 day duration	40 fragments per 1 GREX-100M flask 11 day duration	- Increased tumor fragments per flask - Shortened culture time - Reduced number of steps - Amenable to closed system
Pre-REP to REP Transition	- Pre-REP TIL are frozen until phenotyped for selection then thawed to proceed to the REP (-day 30) - REP requires $>40 \times 10^6$ TIL	- Pre-REP TIL directly move to REP on day 11 - REP requires $25-200 \times 10^6$ TIL	- Shortened pre-REP-to-REP process - Reduced number of steps - Eliminated phenotyping selection - Amenable to closed system
REP	6 GREX-100M flasks on REP day 0 5×10^6 TIL and 5×10^8 PBMC feeders per flask on REP day 0 - Split to 18-36 flasks on REP day 7 14 day duration	1 GREX-500M flask on day 11 $25-200 \times 10^6$ TIL and 5×10^9 PBMC feeders on day 11 - Split to ≤ 6 GREX-500M flasks on day 16 11 day duration	- Reduced number of steps - Shorter REP duration - Closed system transfer of TIL between flasks - Closed system media exchanges
Harvest	TIL harvested via centrifugation	TIL harvested via LOVO automated cell washing system	- Reduced number of steps - Automated cell washing - Closed system - Reduced loss of product during wash
Final Formulation	- Fresh product in Hypothermosol - Single infusion bag - Limited shipping stability	- Cryopreserved product in PlasmaLyte-A + 1% HSA and CS10 stored in LN₂ - Multiple aliquots - Longer shipping stability	- Shipping flexibility - Flexible patient scheduling - More timely release testing
Overall Estimated Process Time	43 -55 days	22 days	Faster turnaround to patient

FIG. 11