Workshop 2: How can we leverage learnings from standard biologics and biosimilars to develop and characterize new biologic and cell/gene therapies?

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Discussion Topics

Topic 1

1. How can prior knowledge be leveraged in process characterization strategies?
2. How lean can we get w/o compromising process performance/product quality - merits of standardization/platform processes
   - Share examples leading to reduction in scale-down studies thus saving time and resources.

Topic 2

3. How does continued improvement in analytical capabilities impact process development?
   - Share examples of any gains observed with advanced analytics
4. Are there game changing PAT tools worth mentioning - real time monitoring, predictive controls, automation, modeling, AI/ML?

Topic 3

5. What can we learn from biosimilar development and how has this informed development of innovative products?
6. How can all the learning impact and help the development of new modalities such as cell and gene therapy?
   - Share examples of any quick wins of prior knowledge that enables to hit the ground running

Proposed Brainstorming Approach

Examples where we can hit the ground running leveraging pior

knowledge

E.g. risk based validation approaches

Examples of where we would have to start from ground up as these may be unchartered territories

E.g. Automation / scale-up for cell isolation, particle clearance in CT

Web links to literatures cited at the workshop

Topic 1

Upstream cell culture process characterization and in-process control strategy development at pandemic speed

Jianlin Xu, Icon, Jianfa Ou, Kyle P. McHugh, Michael C. Borys & Anurag Khetan

- Figure 2 shares examples of the reduction in Process characterization studies in accelerated timeline

Topic 2

Leveraging rAAV bioprocess understanding and next generation bioanalytics development

Jose M Escandell, Daniel AM Pais, Sofia B Carvalho, Karen Vincent, Patrícia Gomes-Alves, Paula M Alves

- Figure 2 demonstrates advanced analytics aid process understanding and reshape development focus

Topic 3

Optimization of the quality by design approach for gene therapy products: A case study for adeno-associated viral vectors

Toshimitsu Tanaka, Hideki Hanaoka, Shingo Sakurai

- Graphical abstract highlights the development scheme adapted from standard biologics.

Topic 1 Discussion Note Highlights

- Prior knowledge used to design PC strategies
  - The need for CPPs and CQA are consistent across modalities
  - Strong need to generate knowledge (data) when none/little exists
  - Front-load PC strategy (analytical, clinical data, etc)

- How lean can we get without compromising quality?
  -Accept that extra studies today can drive a leaner process with time
  -Less business risk by starting PC earlier (more confidence in success after PhI)
  -Build on early data sets to build orthogonal approaches (PAT tools, AI, Machine learning, etc)

- Similar Framework -> CQAs for QTPP, use FMEA-based risk assessment on Unit op

Topic 2 Discussion Notes Highlights

- Continued improvement in analytical capabilities impact process development
  - ❖ Use more inline/online tools that is consistent, reliable, easy to use and fast!
  - ❖ broad multiplex data (e.g., mass spec)
  - ❖ data flows directly to ELNs
  - ❖ scalable tools: microscale ambr to 2000 L brx
  - ❖ small volume input to assay
  - ❖ Develop better product quality tools (e.g. methods for empty/ full capsids)
  - ❖ getting the right type of info and reduced sampling to minimize contamination risks

- Game-changing PAT tools -> simple and facility-friendly for the future
  1. Biocapacitance
  2. Raman

Topic 3 Gene/Cell Therapy Application

- Understanding product quality impact
- No prior knowledge available, but can prior knowledge bias understandings?
- Identifications of CQA and CPP requires iteration -> Don’t rush!
- Ask the right questions by identifying right CQAs, which need confident in analytical method.
- Leverage potency assay to guide CQA determination

- Scale up/down with transient transfection
- unit ops similar to biologics; can leverage same control strategies
- focus more on things that are different between the two

- Increased info sharing in bioforum - not yet biosimilar in GTx/CTx space
- To increase speed -> need clean data sets with standardization
- Better guidelines for cell banking - viewing cells as drug substance

- Reducing cost strategies in biologics haven't been applied to GTx/CTx

- Improving GMP-grade raw materials is critical to success
- SDM are a challenge - No roadmap for Allo and iPSC
- PC per unit op, linkage @ the end—> Can inform iPSCs

Q16 Indicate your top interests (1 top + 2 backups) among the 8 bullets included below:

Answered: 49 Skipped: 280

ANSWER CHOICES	RESPONSES	
How can prior knowledge be leveraged in process characterization strategies?	57.14%	28
Share examples leading to reduction in the number of scale-down studies thus saving time and resources	44.90%	22
How lean can we get w/o compromising process performance/product quality - merits of standardization/platform processes	59.18%	29
How does continued improvement in analytical capabilities impact process development?	30.61%	15
Are there game changing PAT tools worth mentioning - real time monitoring, predictive controls, automation, modeling, AI/ML?	26.53%	13
What can we learn from biosimilar development and how has this informed development of innovative products?	40.82%	20
How can all the learning impact and help the development of new modalities such as cell and gene therapy?	46.94%	23

#	HOW CAN PRIOR KNOWLEDGE BE LEVERAGED IN PROCESS CHARACTERIZATION STRATEGIES?	DATE
1	2	4/14/2023 2:00 PM
2	BU	4/14/2023 1:16 PM
3	1	4/14/2023 9:12 AM
4	1	4/14/2023 7:51 AM
5	1	4/13/2023 5:00 PM
6	Backup 1	4/13/2023 4:47 PM
7	#2	4/13/2023 4:26 PM
8	1	4/13/2023 4:23 PM
9	Backup	4/13/2023 4:01 PM
10	BACKUP	4/13/2023 3:49 PM
11	3	4/13/2023 3:42 PM
12	1	4/13/2023 3:35 PM
13	1	4/7/2023 12:22 PM
14	backups	4/5/2023 3:56 PM
15	top	4/5/2023 3:02 PM
16	top	4/4/2023 8:09 AM
17	backup	4/4/2023 1:12 AM
18	backup	4/3/2023 11:49 AM
19	Back-up	4/3/2023 9:47 AM
20	2	4/3/2023 2:40 AM
21	3	4/2/2023 4:58 PM

22	1	4/2/2023 4:40 PM
23	2	4/1/2023 8:35 AM
24	1	3/31/2023 6:45 PM
25	backup	3/31/2023 6:36 PM
26	1	3/31/2023 6:09 PM
27	Top 1	3/31/2023 5:48 PM
28	backup	3/31/2023 5:20 PM
#	**SHARE EXAMPLES LEADING TO REDUCTION IN THE NUMBER OF SCALE-DOWN STUDIES THUS SAVING TIME AND RESOURCES**	**DATE**
1	top	4/14/2023 7:03 PM
2	4	4/14/2023 2:00 PM
3	Top	4/14/2023 1:16 PM
4	2	4/14/2023 9:12 AM
5	Backup 2	4/14/2023 8:32 AM
6	1	4/14/2023 6:23 AM
7	Top	4/13/2023 4:47 PM
8	#1	4/13/2023 4:26 PM
9	1	4/13/2023 4:23 PM
10	TOP	4/13/2023 3:49 PM
11	1	4/13/2023 3:42 PM
12	2	4/7/2023 12:22 PM
13	backup	4/5/2023 3:02 PM
14	1	4/4/2023 11:15 AM
15	backup	4/4/2023 8:09 AM
16	1	4/3/2023 1:47 PM
17	1	4/2/2023 4:58 PM
18	BU	4/2/2023 6:31 AM
19	1	4/1/2023 10:18 AM
20	BU	4/1/2023 3:03 AM
21	top	3/31/2023 6:36 PM
22	2	3/31/2023 6:04 PM
#	**HOW LEAN CAN WE GET W/O COMPROMISING PROCESS PERFORMANCE/PRODUCT QUALITY - MERITS OF STANDARDIZATION/PLATFORM PROCESSES**	**DATE**
1	5	4/14/2023 2:00 PM
2	3	4/14/2023 9:12 AM
3	Top	4/14/2023 8:32 AM
4	2	4/14/2023 7:51 AM
5	Backup 2	4/13/2023 4:47 PM
6	#3	4/13/2023 4:26 PM

7	1	4/13/2023 4:23 PM
8	1	4/13/2023 4:01 PM
9	BACKUP	4/13/2023 3:49 PM
10	2	4/13/2023 3:42 PM
11	2	4/13/2023 3:35 PM
12	3	4/13/2023 10:58 AM
13	2	4/7/2023 12:22 PM
14	backup	4/5/2023 3:02 PM
15	Backup	4/5/2023 4:35 AM
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22	BU	4/2/2023 6:31 AM
23	3	4/1/2023 11:57 AM
24	BU	4/1/2023 3:03 AM
25	2	3/31/2023 6:45 PM
26	backup	3/31/2023 6:36 PM
27	1	3/31/2023 6:09 PM
28	3	3/31/2023 5:11 PM
29	1	3/31/2023 4:56 PM

#	HOW DOES CONTINUED IMPROVEMENT IN ANALYTICAL CAPABILITIES IMPACT PROCESS DEVELOPMENT?	DATE
1	7	4/14/2023 2:00 PM
2	3	4/14/2023 7:51 AM
3	2	4/13/2023 5:00 PM
4	2	4/13/2023 4:23 PM
5	1	4/7/2023 12:22 PM
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7	1	4/3/2023 11:09 AM
8	backup	4/3/2023 10:35 AM
9	2	4/3/2023 2:40 AM
10	2	4/2/2023 4:58 PM
11	2	4/2/2023 4:40 PM
12	2	4/1/2023 8:35 AM
13	1	4/1/2023 5:42 AM
14	1	3/31/2023 6:04 PM

15	3	3/31/2023 4:56 PM
#	ARE THERE GAME CHANGING PAT TOOLS WORTH MENTIONING - REAL TIME MONITORING, PREDICTIVE CONTROLS, AUTOMATION, MODELING, AI/ML?	DATE
1	backup	4/14/2023 7:03 PM
2	6	4/14/2023 2:00 PM
3	Backup 1	4/14/2023 8:32 AM
4	2	4/14/2023 6:23 AM
5	1	4/13/2023 4:23 PM
6	Backup	4/13/2023 4:01 PM
7	top	4/5/2023 3:56 PM
8	1	4/4/2023 10:07 AM
9	Back-up	4/3/2023 9:47 AM
10	3	4/2/2023 4:40 PM
11	2	4/1/2023 10:18 AM
12	2	3/31/2023 6:45 PM
13	backup	3/31/2023 5:20 PM
#	WHAT CAN WE LEARN FROM BIOSIMILAR DEVELOPMENT AND HOW HAS THIS INFORMED DEVELOPMENT OF INNOVATIVE PRODUCTS?	DATE
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2	2	4/13/2023 4:23 PM
3	2	4/13/2023 3:35 PM
4	1	4/13/2023 10:58 AM
5	Development allows finding critical points that serve as controls when producing any product on a large scale.	4/10/2023 8:27 PM
6	1	4/7/2023 12:22 PM
7	Backup	4/5/2023 4:35 AM
8	2	4/4/2023 11:15 AM
9	2	4/4/2023 10:07 AM
10	backup	4/4/2023 1:12 AM
11	top	4/3/2023 11:49 AM
12	Back up	4/2/2023 11:38 AM
13	Top	4/2/2023 6:31 AM
14	2	4/1/2023 11:57 AM
15	Top	4/1/2023 3:03 AM
16	1	3/31/2023 6:09 PM
17	Back up 2	3/31/2023 5:48 PM
18	top	3/31/2023 5:20 PM
19	2	3/31/2023 5:11 PM
20	2	3/31/2023 4:56 PM
#	HOW CAN ALL THE LEARNING IMPACT AND HELP THE DEVELOPMENT OF NEW	DATE

	MODALITIES SUCH AS CELL AND GENE THERAPY?	
1	backup	4/14/2023 7:03 PM
2	1	4/14/2023 2:00 PM
3	BU	4/14/2023 1:16 PM
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7	1	4/13/2023 3:35 PM
8	2	4/13/2023 10:58 AM
9	2	4/7/2023 12:22 PM
10	backups	4/5/2023 3:56 PM
11	Top	4/5/2023 4:35 AM
12	2	4/4/2023 11:15 AM
13	3	4/4/2023 10:07 AM
14	Top	4/4/2023 1:12 AM
15	2	4/3/2023 1:47 PM
16	3	4/3/2023 11:09 AM
17	top	4/3/2023 10:35 AM
18	Top	4/3/2023 9:47 AM
19	1	4/1/2023 11:57 AM
20	1	4/1/2023 8:35 AM
21	2	3/31/2023 6:45 PM
22	Back up 1	3/31/2023 5:48 PM
23	1	3/31/2023 5:11 PM