Table 4: Considerations for Placing Mass Spec in the High-throughput Lab

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Scope:
The biopharmaceutical industry is moving drug programs to proof of concept at a faster pace by accelerating more molecules through discovery, cell line development and other early development activities. This acceleration has increased demands on analytical functions to screen for lead therapeutic candidates, ruling out cell lines with undesired attributes.

Application of mass spectrometry (MS) to characterize protein therapeutics with molecular details has become standard practice in the industry, while technical challenges remain in the MS-based screening of larger compound libraries. Some of these are lengthy and costly sample preparation stages, followed by low throughput LC-MS/MS methods and lack of software analysis tools. With regard to integrated high-throughput MS systems currently commercially available, there are few options except the most well-known Agilent RapidFire 365. Discussions on the system considerations/requirements would facilitate users to select/build the proper system to address their specific needs.

Questions for Discussion:

1. What are the main goals of placing mass spec in high-throughput lab, which was not achieved by traditional screening?
2. What conference attendances most want to analyze using MS-based screening assays?
3. What are the common sample introduction and sample preparation systems that have been used currently for the high-throughput screening?
4. What are the preferred vendors of MS detection system?
5. What are the software solutions for data analysis and report generation?
6. What are the limitations of the MS-based screening? What are the future needs?

Discussion Notes:

Attendees (9)

Attendees:

- 5 from Pharmaceutical companies
- 2 instrument vendors
- 1 postdoc
- 1 software company

1. What are the main goals of placing mass spec in high-throughput lab, which was not achieved by traditional screening?
    - To screening large volume of samples (mini bioreactors)
    - To enable fast and reliable data analysis
    - To be equipped with automated sample prep robots, and increase throughput

2. What conference attendances most want to analyze using MS-based screening assays?

    - Large molecule
    - siRNA, 50KD-200KD;
    - screening for small molecules

3. What are the common sample introduction and sample preparation systems that have been used currently for the high-throughput screening?
    - Manual sample preparation, inline MALS,
    - Nunc mini trays
    - System suitability self-check

4. What are the preferred vendors of MS detection system?
    - Empower HIC

5. What are the challenges for lab execution and data analysis of high-throughput MS and possible solution to improve day-to-day data precision? (software solutions?)
    - Challenges:
        - Data could be inconsistent, from plate to plate, (using Skyline for data analysis)
        - Thousands of lysate samples through the SPE. Lab need to change the SPE frequently
    - Possible solutions
        - Two stage digestion by LysC and trypsin to ensure accuracy
        - Running on LS1 autosampler, using multi-channel pipets
        - Using other small molecule/caffeine as a reference standard
        - Use product reference standard as the internal standard

6. What are the limitations of the MS-based screening? What are the future needs?

    - Throughput defined by the separation. With that limitation, what kind of throughput can you handle?
    - If multiple projects are going on, it is hard to find enough time/source to develop a good MS method.
    - Data analysis software
    - IT support/data scientist