

BIOPHARMA

TRENDS



2018–2019

TRENDS IN BIOPHARMA MANUFACTURING SURVEY REPORT

Sponsored by NIBRT and The Medicine Maker (Texere Publishing)
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EXECUTIVE SUMMARY

This report summarizes the results of an online survey conducted by the National Institute for Bioprocessing Research and Training (NIBRT) and The Medicine Maker (a Texere Publication) to learn more about current manufacturing practices and trends in the biopharma industry. The survey was fielded from 21 December 2018 to 18 February 2019. During the time that this survey was open, 151 qualified surveys were collected which served as the basis for this report.

DEMOGRAPHICS

Seventy-eight percent (78%) of the survey respondents were located in Europe; 10% were in Asia, Australia, Pacific Rim; and 8% were in North America. The remaining 4% were located in South Africa.

Forty-six percent (46%) of the respondents worked for biopharma manufacturers, 12% worked for contract service providers, and 10% were consultants. Fourteen percent (14%) were affiliated with academic institutions, 7% worked for suppliers/vendors, and 4% worked in government organizations.

One-half (52%) of the industry survey respondents who worked in biopharma manufacturing or for contract service providers worked in large companies. Twenty-eight percent (28%) worked in medium-size companies. And 18% worked in small companies or start-ups.

The most common focus for respondents' organizations was monoclonal antibodies (mAbs) (65%), followed by non-mAb recombinant proteins (40%). Antibody drug conjugates (29%), gene therapies (25%), cell therapies (24%), and vaccines (23%) were cited less often. RNA-based therapies were a focus for 10% of these organizations.

Three-fifths (60%) of the survey respondents had 10 or more years of work experience. Twenty-seven percent (27%) had 3 to 9 years of work experience and 12% had 1 to 2 years of work experience. The remaining 1% of the respondents had no work experience.

KEY FINDINGS

THE PRODUCT PIPELINE

The most commercially important biopharma therapeutic product that was currently available was mAbs (80%), followed by vaccines (51%) and non-mAb recombinant proteins (36%). The remaining products were cited less often: antibody drug conjugates (23%), cell therapies (18%), gene therapies (18%), and RNA-based therapies (9%).

Regarding the biopharma therapeutic products that were likely to be the most important in the next 5 to 10 years, survey respondents most often cited gene therapies (66%), mAbs (58%), and cell therapies (52%). Antibody drug conjugates (30%), vaccines (20%), RNA-based therapies (14%), and non-mAb recombinant proteins (9%) were cited less often.

Monoclonal Abs, antibody drug conjugates, and RNA-based therapies were expected to be of similar importance now and in the next 5 to 10 years. Cell therapies, gene therapies, and vaccines were expected to be more important in the next 5 to 10 years. Non-mAb recombinant proteins were expected to be less important in the next 5 to 10 years.

The issues that respondents felt were the most challenging with regard to bringing new biopharma therapies to market were the scientific complexities in discovering effective therapies for unmet medical needs (80%) and the duration and cost of the drug discovery process (74%). Gaining regulatory approval (61%), pricing models for new products (50%), and cost-effective manufacturing and supply chain methods (46%) were considered less challenging.

Survey respondents felt that the main barriers to more widespread adoption of cell and gene therapies were the scientific complexity/immature nature of the field (70%), regulatory uncertainty (57%), inefficient manufacturing processes/lack of turnkey solutions (44%), and issues with pricing and reimbursement (44%). Supply chain/logistical challenges (21%) and a lack of infrastructure (19%) were cited less often.

By far, the most often cited recent therapeutic innovation was cell and gene therapy, being cited by 79% of the survey respondents; CAR T-cell therapy and CRISPR-Cas9 gene editing were mentioned specifically. Fourteen percent (14%) felt that antibody drug conjugates were the most exciting recent innovation.

MANUFACTURING

Survey respondents felt that the highest priority areas of biopharma manufacturing for further innovation were cell line development and optimization (54% high rating), downstream processing (49%), and bioanalytical capabilities (47%). Aseptic manufacturing and fill-finish technologies (36%), upstream processing (32%), and supply chain logistics (26%) were cited less often.

Respondents thought that automation of manufacturing processes (57% high rating), single-use technologies (56%), data analytics and digitalization (54%), and continuous manufacturing (48%) would have the greatest impact on biopharma manufacturing in the next five years. New expression platforms (37%) and Industry 4.0 technologies (34%) were expected to have less impact.

KEY FINDINGS

Regarding issues with single-use technologies, survey respondents rated lack of standardization as being the most challenging (54%), followed by consistent supply of consumables (43%), cost of consumables (40%), and the limited scale of single-use technologies (38%). Issues with extractables and leachables (30%) and the physical robustness of the single-use bag (30%) were rated as less challenging.

Respondents considered most of the challenges that were related to the continuous manufacturing of biopharmaceuticals to be fairly substantial obstacles, with 44% to 54% rating the following areas as being major obstacles: challenges in the process development of continuous manufacturing processes (54%), still being an unproven technology for biopharma (49%), challenges in the tech transfer of continuous manufacturing processes (45%), regulatory uncertainties (45%), and a lack of real-time monitoring technologies (44%).

The technologies that were considered to be the most relevant with regard to implementation of Industry 4.0 were smart sensors (71%); data analytics, cloud computing, computer simulation, modeling (67%); and robotics and co-robotics, intelligent automation (64%). Cybersecurity (51%), machine learning (44%), and artificial intelligence applications (43%) were cited less often. Augmented and virtual reality (26%) and additive manufacturing (22%) were cited least often.

The biggest challenges cited with regard to biopharma manufacturing were process robustness (59% considered this a major challenge) and process reproducibility (56%). Product yield optimization (46%) and product characterization (42%) were considered to be somewhat less challenging. Supply chain management (25%) and aggregation issues (22%) were considered to be the least challenging issues.

STAFF DEVELOPMENT

A majority (78%) of the survey respondents had difficulty filling one or more positions. Respondents had the most difficulty hiring bioprocess engineers (45%), followed by automation engineers (33%), manufacturing science and technology staff (29%), downstream processing staff (28%), and CQ&V engineers (27%).

The most important skill set for new hires was identified as scientific, engineering, and technical skills (80%). The remaining skill sets were each considered quite important by 52% to 61% of the respondents: business skills, such as communication or team work (61%), emotional intelligence competencies (52%), and prior experience in a GMP environment (52%).

The most effective types of training were practical training in a lab and/or pilot plant environment (84%) and on-the-job training (82%). An accredited post-graduate education program from a higher-level education institute was considered less effective (50%). Classroom training (31%), a 1- or 2-day course from a third-party provider on a particular topic (28%), and online training (21%) were considered to be the least effective types of training.

KEY FINDINGS

OPPORTUNITIES AND CHALLENGES

The biggest challenge for the growth of the biopharma industry concerned staff, technical skills (46%). Other responses were cited less often: sales and marketing (14%), funding (12%), costs/product pricing (10%), and R&D/new products (10%).

The biggest opportunities for the growth of the biopharma industry concerned new technologies (27%) and R&D, new products (21%). Other responses were cited somewhat less often: cell and gene therapy (15%); manufacturing (12%); staff, training (12%); and IT/data analytics (8%).

A majority (85%) of the survey respondents were very optimistic (61%) or moderately optimistic (24%) for the future growth of the biopharma industry. Five percent (5%) were neutral and 8% were somewhat pessimistic (4%) or highly pessimistic (4%). The remaining 2% were not sure.

HIGHLIGHTS OF THREE-YEAR TRENDS

DEMOGRAPHICS

The location of survey respondents was not tracked in the 2016 survey. In the 2017 survey there were fewer respondents from Europe and more respondents from North America and Asia, Australia, Pacific Rim (in the 2017 survey, 45% were from Europe, 35% were from North America, and 16% were from Asia, Australia, Pacific Rim).

A much larger percentage of survey respondents in the 2017 and 2018 surveys (46% and 57%) were working in biopharma manufacturing compared to the 2016 survey (38%).

Respondents in the 2017 and 2018 surveys were more experienced than those in the 2016 survey: 45% had 10 or more years of work experience in 2016, 65% had 10 or more years of experience in 2017, and 60% had 10 or more years of experience in 2018. Years of work experience was similar for the 2017 and 2018 surveys.

MOST COMMERCIALY IMPORTANT BIOPHARMA THERAPEUTICS IN THE NEXT 5 TO 10 YEARS

Monoclonal Abs was in the top three responses for each of these years. Gene therapies and cell therapies were in the top three responses for 2017 and 2018. Though vaccines were cited most often in the 2016 survey, they were ranked much lower in the 2017 and 2018 surveys.

PRIORITIES FOR FURTHER INNOVATION IN BIOPHARMA MANUFACTURING

Cell line development, downstream processing, and bioanalytical capabilities have remained among the top three priorities for further innovation for the three years. Bioanalytical capabilities appears to be trending downward in importance (61% high importance in 2016, 57% in 2017, and 47% in 2018).

IMPACT OF TECHNOLOGIES ON BIOPHARMA MANUFACTURING IN THE NEXT FIVE YEARS

Automation of the manufacturing process is trending upward in the level of impact on biopharma manufacturing expected in the next five years (47% high level of impact in 2016, 49% in 2017, and 57% in 2018).

ISSUES WITH SINGLE-USE TECHNOLOGIES

A lack of standardization was considered one of the top challenges in all three surveys (58% major challenge in 2016, 48% in 2017, and 54% in 2018). The cost of consumables was in the top three responses in the 2017 and 2018 surveys (it was not asked in 2016). Several attributes appear to be trending downward over time in being considered technical challenges with regard to single-use technologies: limited scale of single-use technologies, issues with extractables and leachables, and robustness of the single-use bag.

HIGHLIGHTS OF THREE-YEAR TRENDS

CHALLENGES FOR BIOPHARMA MANUFACTURING

The issues or key challenges identified with regard to biopharma manufacturing have been similar over the last three surveys. One modest change concerns a slight downward trend in the level of challenge for supply chain management: 34% considered it a major challenge in 2016, 28% did so in 2017, and 25% did so in 2018.

CHALLENGES WITH CONTINUOUS MANUFACTURING

Challenges in the development of continuous manufacturing processes has been the most often cited major challenge in all three surveys. In contrast, regulatory uncertainties and a lack of real-time monitoring technologies appear to be trending downward in terms of being major challenges. Three-fifths (60%) considered regulatory uncertainties a major challenge in 2016, 49% did so in 2017, and 45% did so in 2018. Fifty-six percent (56%) considered a lack of real-time monitoring technologies a major challenge in 2016, 52% did so in 2017, and 44% did so in 2018.

STAFF DEVELOPMENT

The importance of various skill sets has remained relatively constant over the three years. One exception concerns the importance of business skills, such as communication or team work, which appears to be considered more important in 2017 and 2018 than in 2016: 39% considered it to be quite important in 2016, 63% did so in 2017, and 61% did so in 2018.

CHALLENGES AND OPPORTUNITIES

Staff, technical skills was considered a major challenge in both the 2017 and 2018 surveys but was cited more often in the 2018 survey (29% cited this as a major challenge in 2017 while 46% did so in 2018). Costs, pricing was considered less of a challenge in 2018 compared to 2017 (29% cited this as a major challenge in 2017 while only 10% did so in 2018).

Regarding opportunities, new technologies, R&D/new products, and cell and gene therapy were the top three responses for both the 2017 and 2018 surveys. New technologies was cited by 16% of the respondents in 2017 and by 27% of the respondents in 2018.

METHODS

The Medicine Maker, a Texere Publication, conducted a web-based survey to learn more about current manufacturing practices and trends in the industry in partnership with the National Institute for Bioprocessing Research and Training (NIBRT). The results of this survey will be published in The Medicine Maker in quarter 1 2019.

This survey has been conducted in the fall or winter of 2016, 2017, and 2018. This report covers the findings from the 2018 survey as well as significant changes or trends over these three years. In general, the survey questions have remained the same; the responses for some questions have been changed or simplified where possible over this time. In particular, some questions where several attributes were rated have been changed to multiple choice questions and some open-ended or fill-in response questions have been changed to multiple choice questions.

Some of the questions for this year's survey were changed from open-ended or fill-in responses to select all that apply responses based on the verbatim responses provided in the previous two surveys. This was done to simplify taking the survey and to reduce the time required to complete the survey.

This survey was fielded from 21 December 2018 through 18 February 2019. During this time, several e-mail bursts were sent to registrants from both NIBRT and Texere databases; other promotional efforts included e-newsletters and social media. A prize draw for one of three 9.7-inch Apple iPads was offered as an incentive to participate.

During the eight weeks that this survey was fielded, 151 surveys were collected from individuals who were involved in biopharmaceutical manufacturing; some of these surveys were only partially completed. These 151 qualified surveys served as the basis for this report. The margin of error for the full set of data is less than +/-8.0% at the 95% confidence level.

RESULTS AND CONCLUSIONS

Each question is presented along with the results and comments. Comparisons are made where there were significant differences in the responses from this year's (2018) survey versus the 2017 and 2016 surveys.

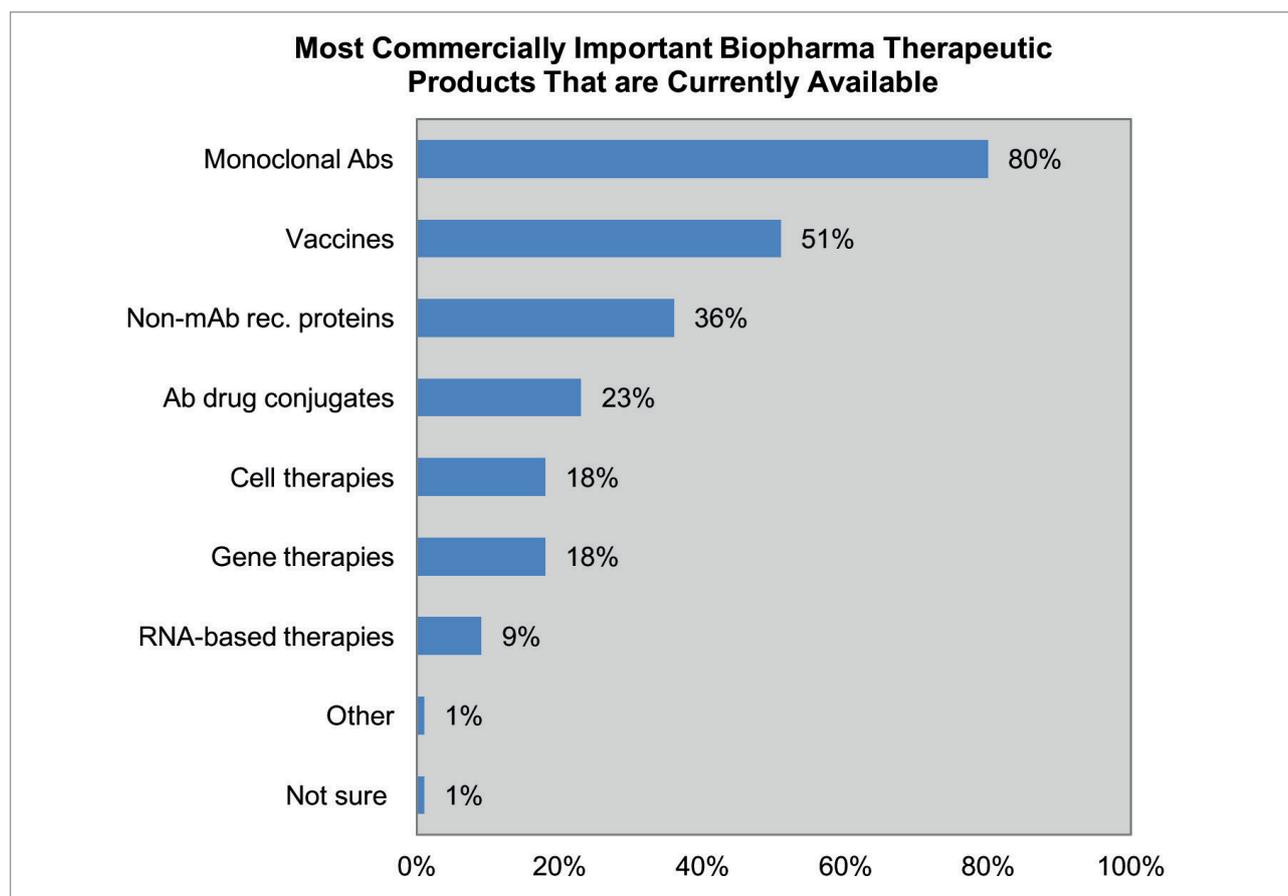
1. *Are you currently involved in biopharmaceutical manufacturing?*

All (100%) of the 151 survey respondents were involved in biopharmaceutical manufacturing.

There were 101 respondents for the 2016 survey and 210 respondents for the 2017 survey.

THE PRODUCT PIPELINE

2. *Please select the most commercially important biopharma therapeutic products that are currently available. (Select up to three)*



Survey respondents were allowed to choose more than one response to this question; therefore the responses total more than 100%. Some responses have been shortened due to space constraints.

RESULTS AND CONCLUSIONS

The most commercially important biopharma therapeutic product that was currently available was monoclonal antibodies (mAbs) (80%), followed by vaccines (51%) and non-mAb recombinant proteins (36%).

The remaining products were cited less often: antibody drug conjugates (23%), cell therapies (18%), gene therapies (18%), and RNA-based therapies (9%).

Other fill-in responses (1%) included antibiotics and bacteriophage therapies.

Individuals who were located in Asia, Australia, Pacific Rim were more likely to cite RNA-based therapies while those located in Europe were less likely to do so.

Individuals who worked for contract service providers were more likely to cite antibody drug conjugates while those working in biopharma companies were less likely to do so.

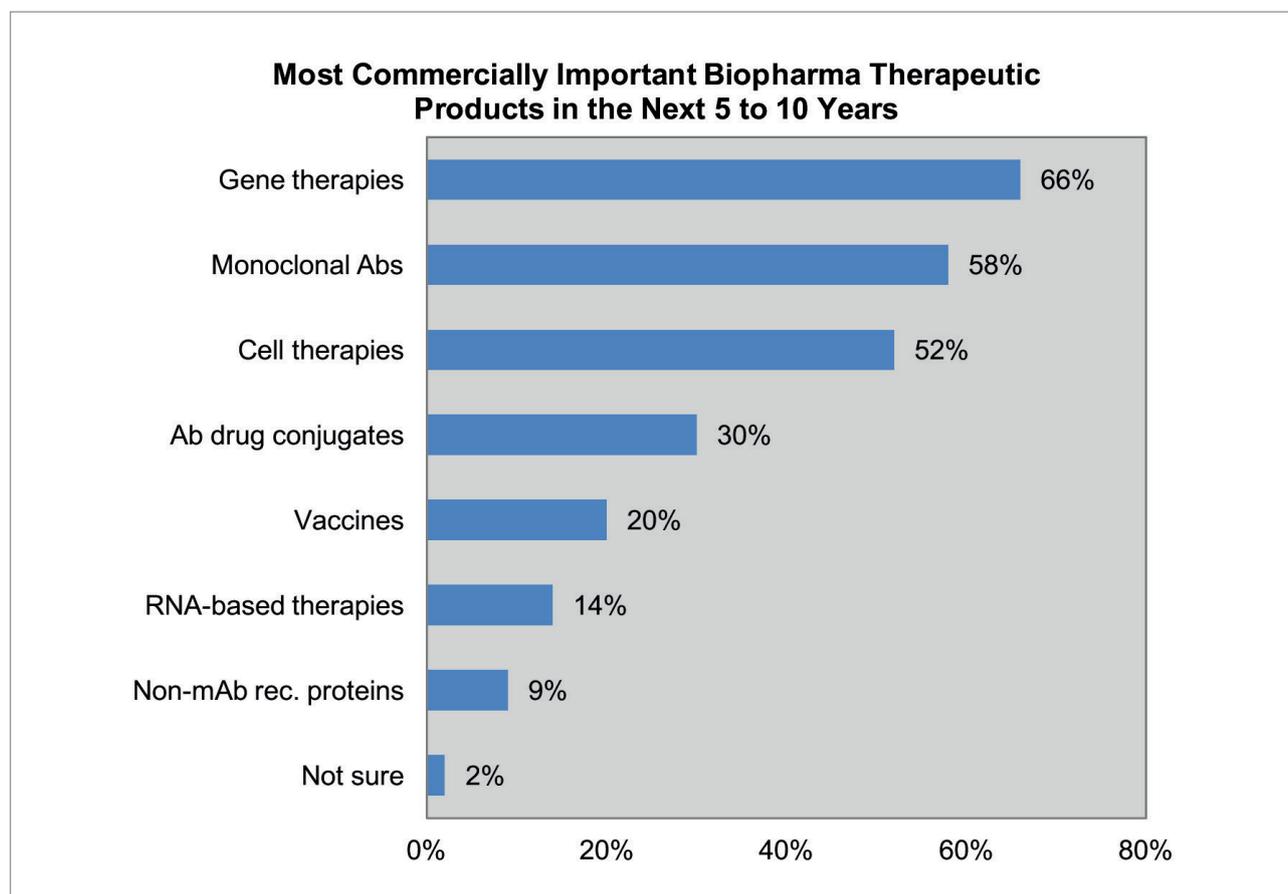
Individuals with 10 or more years of work experience were more likely to cite non-mAb recombinant proteins. Those with less than 10 years of experience were more likely to cite RNA-based therapies.

It is important to note that survey respondents tended to consider the primary focus of their organization (see question 32) to be the most commercially important products currently available.

In general, the ranking for these responses has been similar over the three years. One slight difference is that cell therapies and gene therapies were considered somewhat more important in the 2016 survey and somewhat less important in the 2017 and 2018 surveys.

RESULTS AND CONCLUSIONS

3. Which of the following are likely to be the most commercially important biopharma therapeutic products in the next 5 to 10 years? (Select up to three)



Survey respondents were allowed to choose more than one response to this question; therefore the responses total more than 100%. Some responses have been shortened due to space constraints.

Regarding the biopharma therapeutic products that were likely to be the most important in the next 5 to 10 years, survey respondents most often cited gene therapies (66%), mAbs (58%), and cell therapies (52%).

Antibody drug conjugates (30%), vaccines (20%), RNA-based therapies (14%), and non-mAb recombinant proteins (9%) were cited less often.

Individuals who were located outside of Europe were more likely to cite vaccines while those in Europe were less likely to do so.

Individuals who worked in biopharma companies, contract service providers, or academe were more likely to cite gene therapies while those working for suppliers/vendors, government organizations, or consulting firms were less likely to do so.

RESULTS AND CONCLUSIONS

It is important to note that survey respondents also tended to consider the primary focus of their organization (see question 32) to be the most commercially important products in the next 5 to 10 years.

The ranking for these responses has changed significantly over the last three surveys. The following table depicts the ranking and percent response for the top three responses by year.

Most Commercially Important Biopharma Therapeutics In The Next 5 To 10 Years: Top Three Responses

<i>Rank</i>	<i>2016*</i>	<i>2017</i>	<i>2018</i>
First	Vaccines (78%)	mAbs (56%)	Gene therapies (66%)
Second	mAbs (68%)	Cell therapies (43%)	mAbs (58%)
Third	Antibody drug conjugates (68%)	Gene therapies (42%)	Cell therapies (52%)

**The rating scale for this question was changed in the 2017 survey so the 2016 figures are not directly comparable to those from the 2017 and 2018 surveys.*

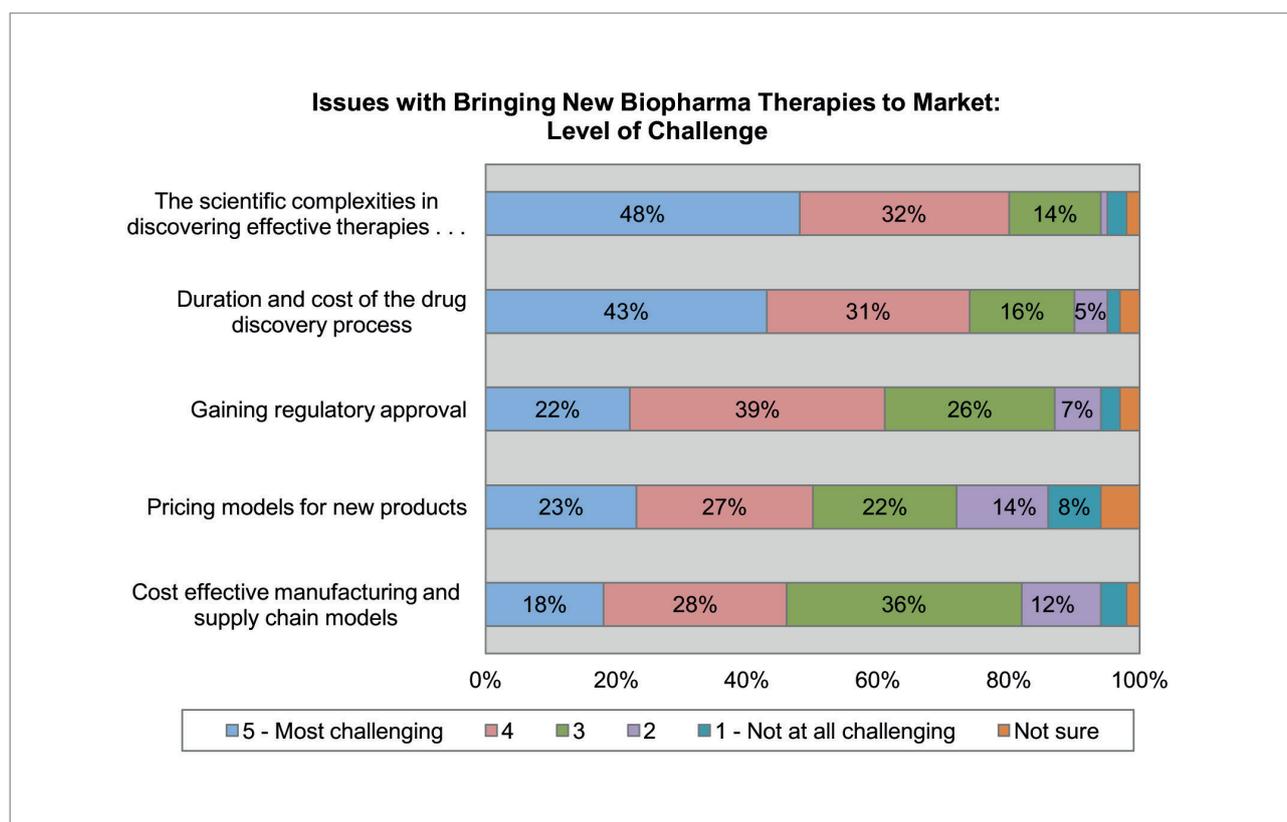
Monoclonal Abs was in the top 3 responses for each of these years. Gene therapies and cell therapies were in the top 3 responses for 2017 and 2018. While vaccines was cited most often in the 2016 survey, it ranked lower in the 2017 and 2018 surveys (ranked 5th in 2017 and 2018).

MOST COMMERCIALY IMPORTANT BIOPHARMA THERAPEUTIC PRODUCTS: NOW VERSUS THE NEXT 5 TO 10 YEARS

Monoclonal Abs, antibody drug conjugates, and RNA-based therapies were expected to be of similar importance now and in the next 5 to 10 years. Cell therapies, gene therapies, and vaccines were expected to be more important in the next 5 to 10 years. Non-mAb recombinant proteins were expected to be less important in the next 5 to 10 years.

RESULTS AND CONCLUSIONS

4. Please rate the following issues as to how challenging each is with regard to bringing new biopharma therapies to the market. (Please use a scale from 1 to 5, with 1 being not at all challenging and 5 being the most challenging.)



The attributes in this graph are listed in descending percentage of a rating of 4 plus 5, with 5 being “most challenging”. The values in each horizontal bar total 100%. Some bar segments with smaller values are not labeled due to space constraints. Attributes containing an ellipsis have been shortened due to space constraints.

The issues that survey respondents felt were the most challenging with regard to bringing new biopharma therapies to market were the scientific complexities in discovering effective therapies for unmet medical needs (80% rating of 4 plus 5, with 5 being most challenging) and the duration and cost of the drug discovery process (74%).

Gaining regulatory approval (61%), pricing models for new products (50%), and cost-effective manufacturing and supply chain methods (46%) were considered less challenging.

Individuals who were located in Asia, Australia, Pacific Rim were more likely to rate pricing models for new products and cost-effective manufacturing and supply chain models as being quite challenging, while those located in Europe and North America were less likely to do so.

RESULTS AND CONCLUSIONS

Individuals who worked in biopharma companies were more likely to rate the duration and cost of the drug discovery process as being quite challenging while those working for contract service providers and in consulting were more likely to cite cost effective manufacturing and supply chain models as being quite challenging.

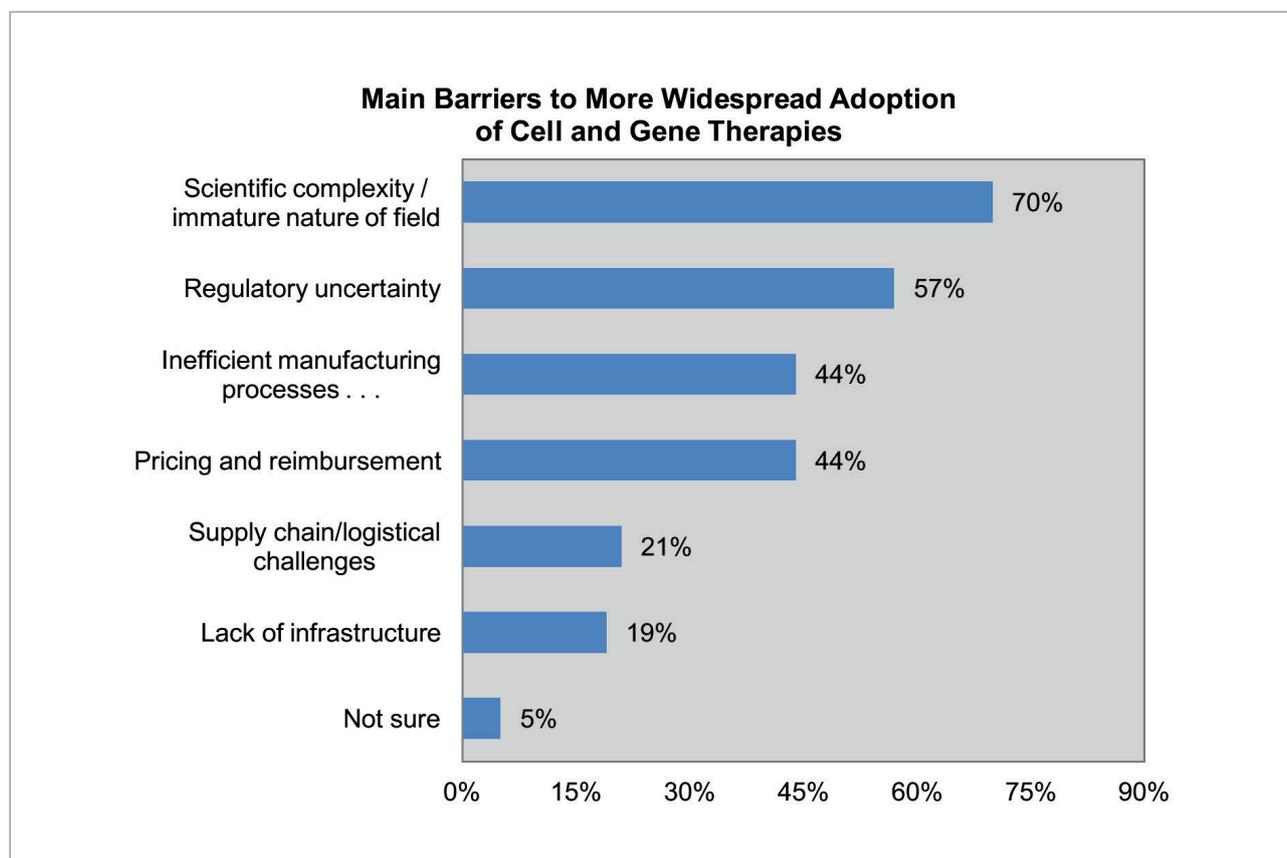
Individuals with 10 or more years of work experience were more likely to rate the scientific complexities in discovering effective therapeutics and the duration and cost of the drug discovery process as being quite challenging while those with less than 3 years of experience were less likely to do so.

Individuals who worked in organizations that primarily focused on antibody drug conjugates were more likely to rate the duration and cost of the drug discovery process as being quite challenging while those who worked in organizations that focused on RNA-based therapies were less likely to do so.

Some of the response options for this question were changed in the 2017 survey to focus on issues that were likely to be more challenging than those measured in the 2016 survey. When the responses that have remained the same over the three years are considered, the ranking and percent response for these attributes have been similar over this time.

RESULTS AND CONCLUSIONS

5. Regarding cell and gene therapies, what are the main barriers to more widespread adoption?
(Select all that apply)



Survey respondents were allowed to select more than one response to this question; therefore the responses total more than 100%.

Survey respondents felt that the main barriers to more widespread adoption of cell and gene therapies were scientific complexity/the immature nature of the field (70%), regulatory uncertainty (57%), inefficient manufacturing processes/lack of turnkey solutions (44%), and issues with pricing and reimbursement (44%).

Supply chain/logistical challenges (21%) and a lack of infrastructure (19%) were cited less often.

Individuals who worked in biopharma companies were more likely to consider scientific complexity/the immature nature of the field to be a main barrier to more widespread adoption of these therapies while those working in consulting were less likely to do so. Those working in consulting were more likely to consider supply chain/logistical challenges and inefficient manufacturing processes to be main barriers while those working for suppliers/vendors or in academe were less likely to do so.

RESULTS AND CONCLUSIONS

Individuals with 10 or more years of work experience were more likely to consider inefficient manufacturing processes and pricing/reimbursement to be major barriers while those with less than 3 years of experience were less likely to do so.

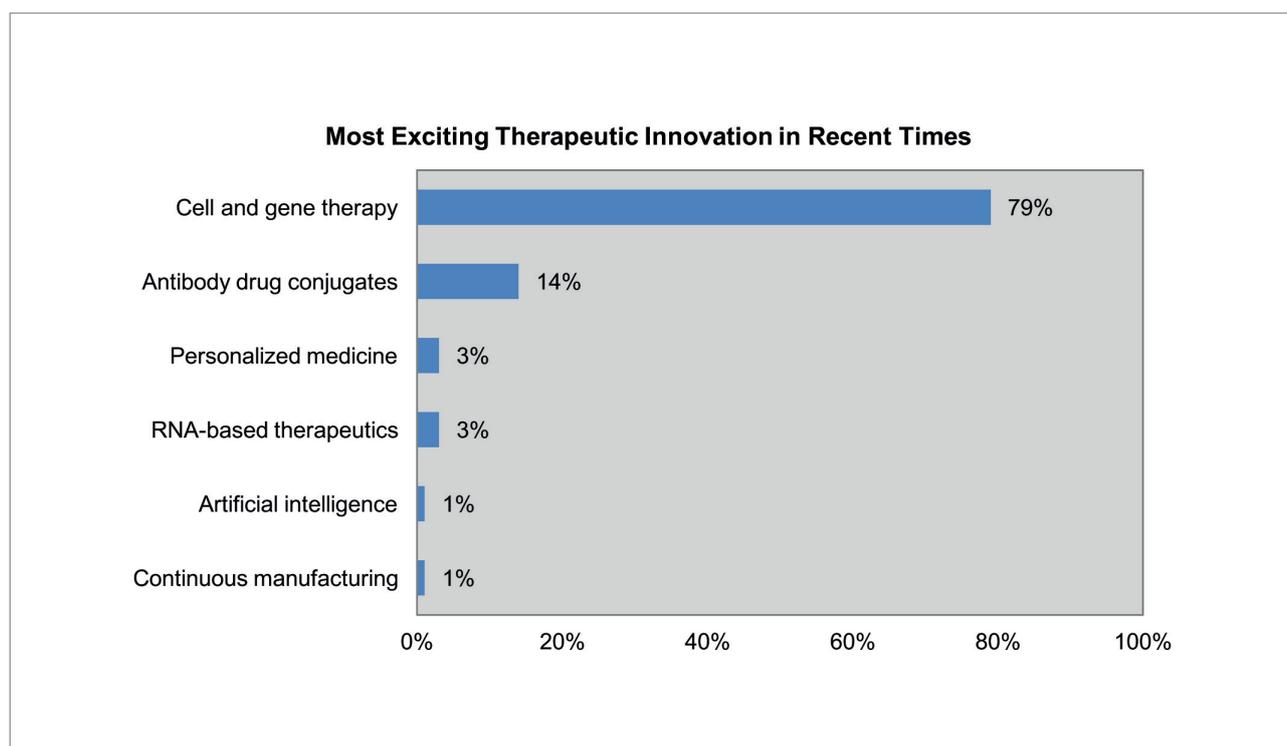
Individuals who worked in organizations that focused primarily on non-mAb recombinant proteins were more likely to consider scientific complexity/the immature nature of the field to be a major barrier while those who worked in organizations that focused on antibody drug conjugates were more likely to consider pricing and reimbursement to be a major barrier to the widespread adoption of cell and gene therapies.

This question was not asked in previous surveys.

RESULTS AND CONCLUSIONS

6. *What has been the most exciting therapeutic innovation in recent times?*

The verbatim responses for this question were categorized to produce the following graph.



Survey respondents were allowed to provide more than one response to this question; therefore the responses total more than 100%.

By far, the most often cited recent therapeutic innovation was cell and gene therapy, being cited by 79% of the survey respondents; CAR T-cell therapy and CRISPR-Cas9 gene editing were mentioned specifically.

Fourteen percent (14%) felt that antibody drug conjugates were the most exciting innovation. The remaining responses were each cited by 3% or fewer respondents.

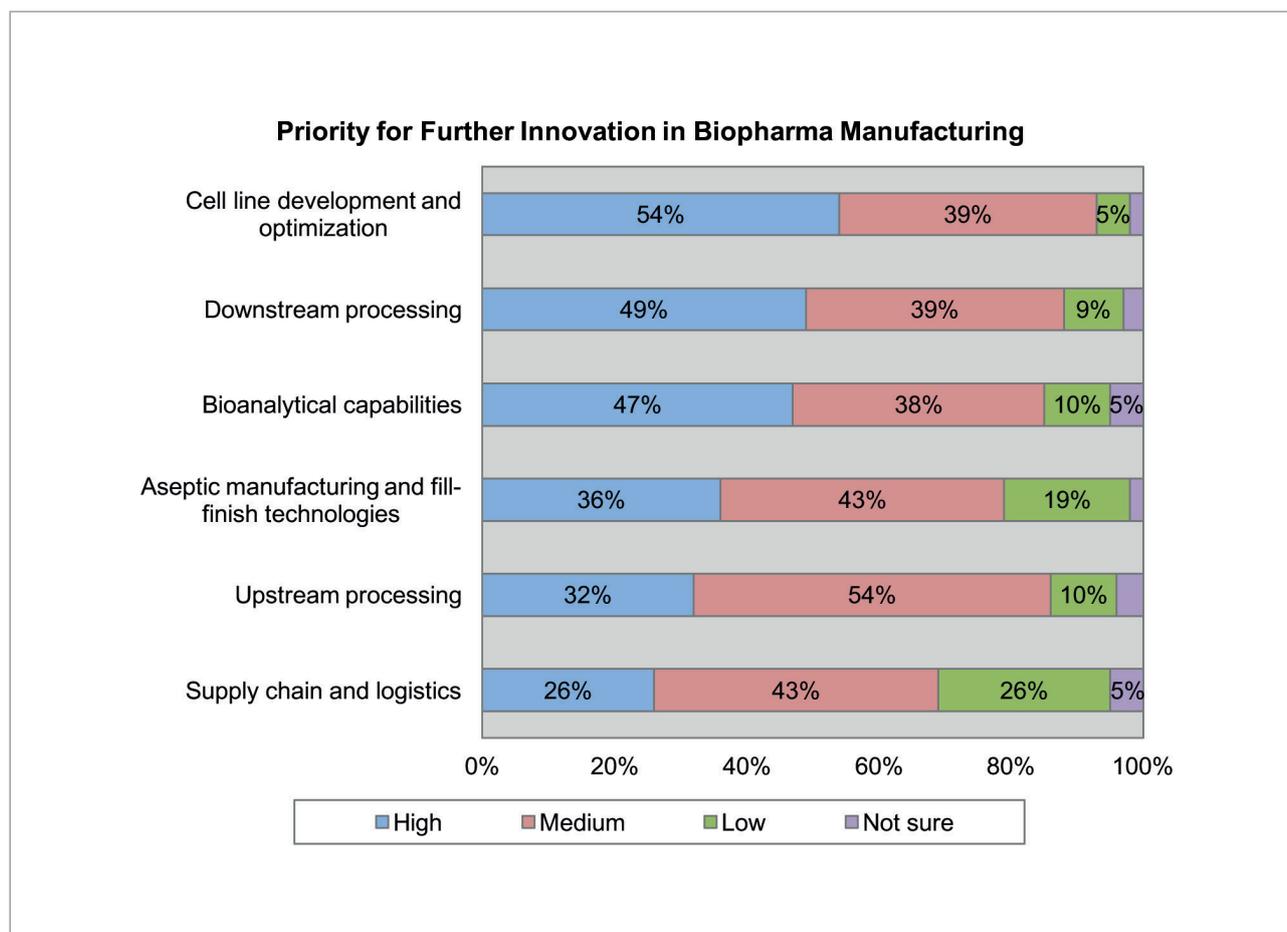
It is interesting to note that survey respondents did not tend to consider the primary focus of their organization (see question 32) to be the most exciting recent therapeutic innovation as was the case for questions 2 and 3.

This question was not asked in the 2016 survey. The responses for this question for the 2017 and 2018 surveys are similar.

RESULTS AND CONCLUSIONS

MANUFACTURING

7. Please rate the priority for further innovation in each of the following areas of biopharma manufacturing.



The attributes in this graph are listed in descending percentage of a “high” rating. The values in each horizontal bar total 100%. Some bar segments with smaller values are not labeled due to space constraints.

Survey respondents felt that the highest priority areas of biopharma manufacturing for further innovation were cell line development and optimization (54% high rating), downstream processing (49%), and bioanalytical capabilities (47%).

Aseptic manufacturing and fill-finish technologies (36%), upstream processing (32%), and supply chain logistics (26%) were cited less often.

Individuals located in Asia were more likely to consider bioanalytical capabilities, aseptic manufacturing and fill-finish technologies, and supply chain and logistics to be a high priority while those located in Europe and North America were less likely to do so.

RESULTS AND CONCLUSIONS

Individuals who worked in consulting firms were more likely to consider bioanalytical capabilities to be a high priority while those working for contract service providers or suppliers/vendors were less likely to do so.

Individuals in organizations that focused primarily on antibody drug conjugates were more likely to consider upstream processing a high priority while those in organizations that focused on cell or gene therapies were less likely to do so.

Cell line development, downstream processing, and bioanalytical capabilities have remained among the top three responses over the three years. Bioanalytical capabilities appears to be trending downwards in importance (61% high importance in 2016, 57% in 2017, and 47% in 2018).

8. *If there are other high priority areas for further innovation that were not listed above, please note them here.*

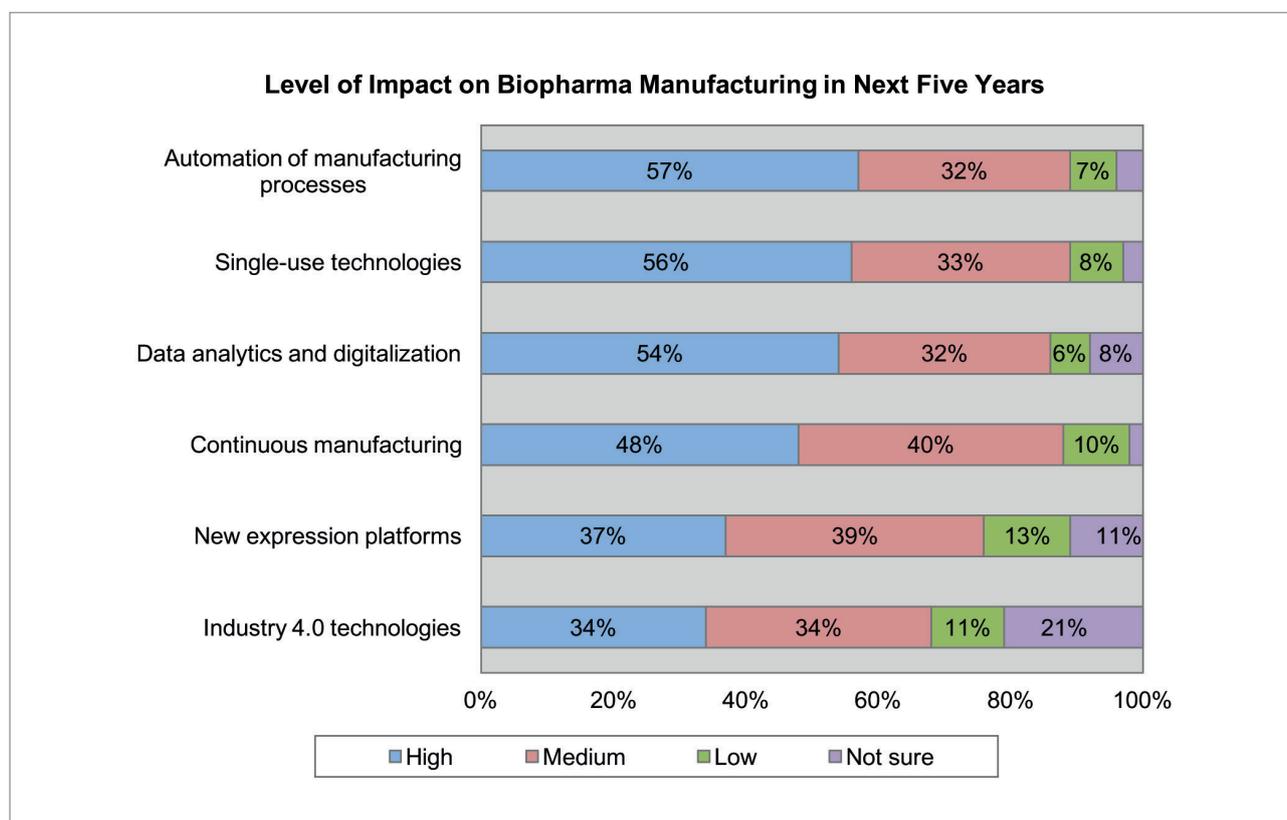
Other areas of high priority for further innovation concerned IT/data integrity, cell and gene therapy, regulation, and several other topics. The table on the following page depicts all of the verbatim responses for this question. These responses are sorted by category or topic.

Other High Priority Areas For Further Innovation

<i>Category</i>	<i>Verbatim Response</i>
IT, data integrity	Application of AI technologies to Biopharma
IT, data integrity	Bioinformatics
IT, data integrity	Connected plant ... digital threads and digital twins
IT, data integrity	Data analytics
IT, data integrity	Data analytics software that pulls electronic information needs to be more user friendly to get the most out of the data that is available. Also needs to be compatible with all electronic instruments
IT, data integrity	Improvement of bioinformatic data management and data analysis
IT, data integrity	Multi variate analysis and the use of data in innovation in research
Cell and gene therapy	CRISPR
Cell and gene therapy	Delocalized consequences of CRISPR
Cell and gene therapy	Gene recognition
Cell and gene therapy	Promoting cell therapies versus the 'norm' (chemo, etc.) at the moment
Regulation	Regulatory affairs
Regulation	Regulatory Agency engagement (ethical and scientific guidelines require updates)
Regulation	Regulatory aspect is of prime importance for consistent in-depth quality assessment of risk involved in immunogenicity response.
Drug delivery	Drug delivery systems
Drug delivery	Oral delivery formats for biopharmaceuticals
Manufacturing	Accelerated production times
Manufacturing	Continuous biopharmaceutical manufacture
Staff, training	Availability of personnel
Staff, training	Training and skills
Other	Clinical trial protocols
Other	Cost control
Other	Disruptive technology
Other	Formulation development
Other	Media makeup

RESULTS AND CONCLUSIONS

9. Please rate each of the following with regard to their impact on biopharma manufacturing in the next five years.



The attributes in this graph are listed in descending percentage of a “high” rating. The values in each horizontal bar total 100%. Some bar segments with smaller values are not labeled due to space constraints.

Automation of manufacturing processes (57% high rating), single-use technologies (56%), data analytics and digitalization (54%), and continuous manufacturing (48%) were thought to have the greatest level of impact on biopharma manufacturing in the next five years.

New expression platforms (37%) and Industry 4.0 technologies (34%) were thought to have less impact on biopharma manufacturing in the next five years.

Individuals located in Asia, Australia, Pacific Rim were more likely to rate Industry 4.0 as having high impact on biopharma manufacturing in the next five years while those located in North America were less likely to do so.

Individuals who worked for contract service providers were more likely to rate automation of manufacturing processes as having high impact; those who worked for suppliers/vendors were more likely to rate continuous manufacturing as having high impact; and those working in consulting were more likely to rate data analytics and digitalization, new expression platforms, and Industry 4.0 technologies as having high impact on biopharma manufacturing in the next five years.

RESULTS AND CONCLUSIONS

Individuals in organizations with their primary focus on antibody drug conjugates were more likely to rate single-use technologies as having high impact. Those in organizations that focused on gene therapies or RNA-based therapies were more likely to rate new expression platforms as having high impact on biopharma manufacturing in the next five years.

Automation of the manufacturing process is trending upwards in the level of impact on biopharma manufacturing expected in the next five years (47% high level of impact in 2016, 49% in 2017, and 57% in 2018). Industry 4.0 technologies was rated in the 2018 survey, but not in previous surveys.

10. If there are other high impact areas that were not listed above, please note them here.

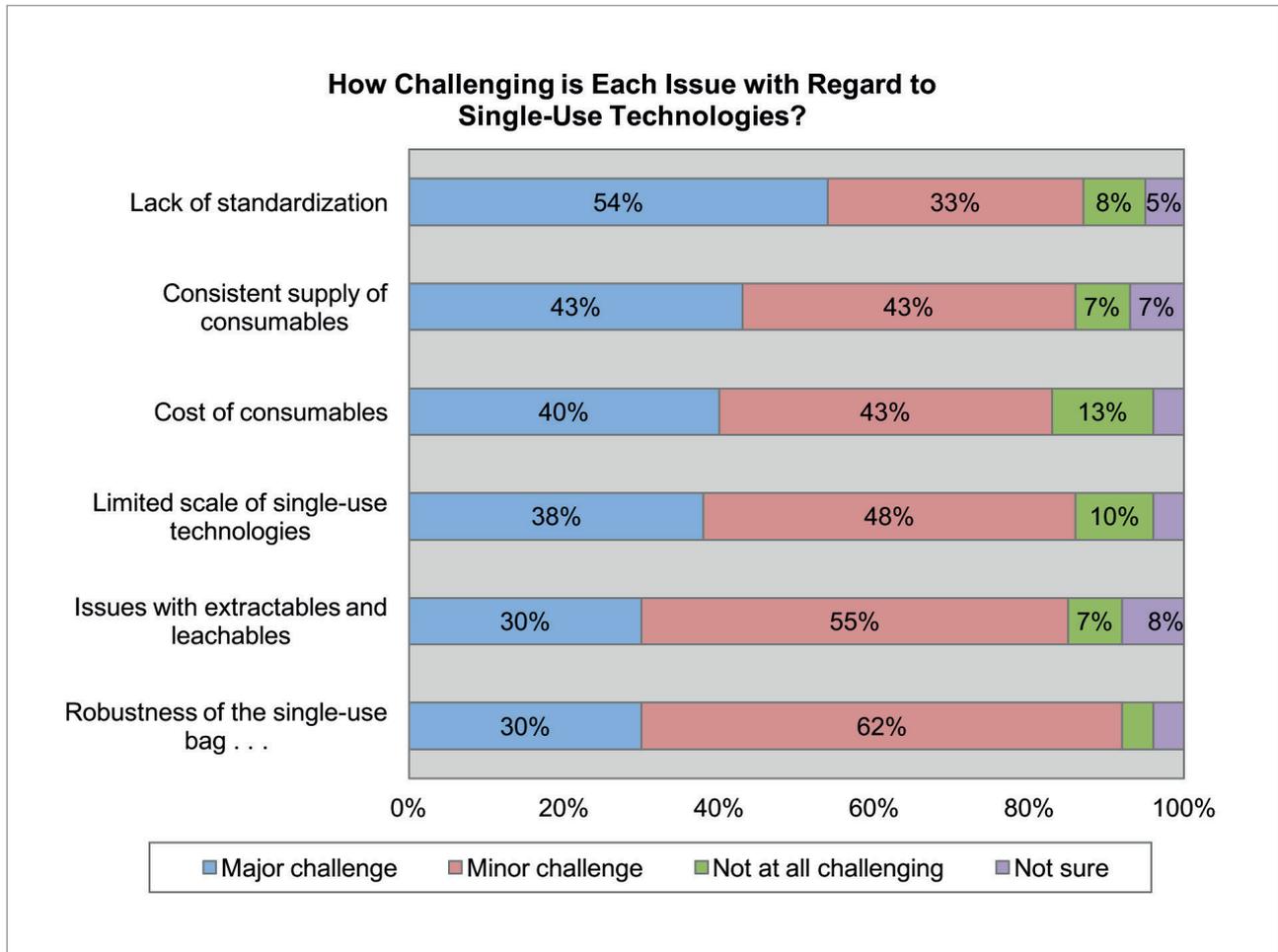
Other areas of high impact on biopharma manufacturing in the next five years concerned new technologies, IT/data integrity, and manufacturing. The following table depicts all of the verbatim responses for this question. These responses are sorted by category or topic.

Other Major Obstacles With Regard To Continuous Manufacturing

<i>Category</i>	<i>Verbatim Response</i>
New technologies	AI-based technologies
New technologies	Analytical technologies capabilities
New technologies	Application of AI techniques to data analytics
New technologies	Application of AI technologies to Biopharma.
New technologies	Artificial intelligence (AI)
New technologies	Self-adjusting offline instruments, i.e., inline pH probes will take their own sample, test on an offline calibrated pH meter, and adjust automatically.
IT, data integrity	Integration of data into work flow management LIMS and MES systems
Manufacturing	Continuous manufacturing lacks the financial resources, yet this is the future of novel innovative ways to treat Rare Diseases
Manufacturing	Distributed (local) manufacturing networks
Manufacturing	Scale up and Scale out concepts

RESULTS AND CONCLUSIONS

11. How challenging is each of the following issues with regard to single-use technologies?



The attributes in this graph are listed in descending percentage of a “major challenge” rating. The values in each horizontal bar total 100%. Some bar segments with smaller values are not labeled due to space constraints. Attributes containing an ellipsis have been shortened due to space constraints.

Regarding various issues with single-use technologies, survey respondents rated lack of standardization as being the most challenging (54% rated it as a major challenge), followed by consistent supply of consumables (43%), cost of consumables (40%), and the limited scale of single-use technologies (38%).

Issues with extractables and leachables (30%) and the physical robustness of the single-use bag (30%) were considered major challenges somewhat less often.

Individuals located in Asia, Australia, Pacific Rim were more likely to rate the cost of consumables and the limited scale of single-use technologies as major challenges while those located in Europe were less likely to do so.

RESULTS AND CONCLUSIONS

Individuals who worked in consulting firms were more likely to rate consistent supply of consumables as a major challenge while those who worked in biopharma companies were less likely to do so. Individuals who worked for suppliers/vendors were more likely to rate issues with extractables and leachables as a major challenge with regard to single-use technologies.

A lack of standardization was considered one of the top challenges in all three surveys (58% major challenge in 2016, 48% in 2017, and 54% in 2018). The cost of consumables was in the top three responses in the 2017 and 2018 surveys (it was not asked in 2016). Several attributes appear to be trending downward over time in being considered technical challenges with regard to single-use technologies: limited scale of single-use technologies, issues with extractables and leachables, and robustness of the single-use bag. The following table shows these downward trends.

*How Challenging Each Issue Is With Regard To Single-Use Technologies: Percent Major Challenge And Rank**

<i>Attribute</i>	<i>2016</i>	<i>2017</i>	<i>2018</i>
Limited scale of single-use technologies	50% (3rd)	44% (3rd)	38% (4th)
Issues with extractables and leachables	65% (1st)	41% (4th)	30% (5th)
The physical robustness of the single-use bag	39% (4th)	32% (5th)	30% (6th)

** Ranks are indicated in parentheses*

RESULTS AND CONCLUSIONS

12. If there are other major challenges with regard to single-use technologies that were not listed above, please note them here.

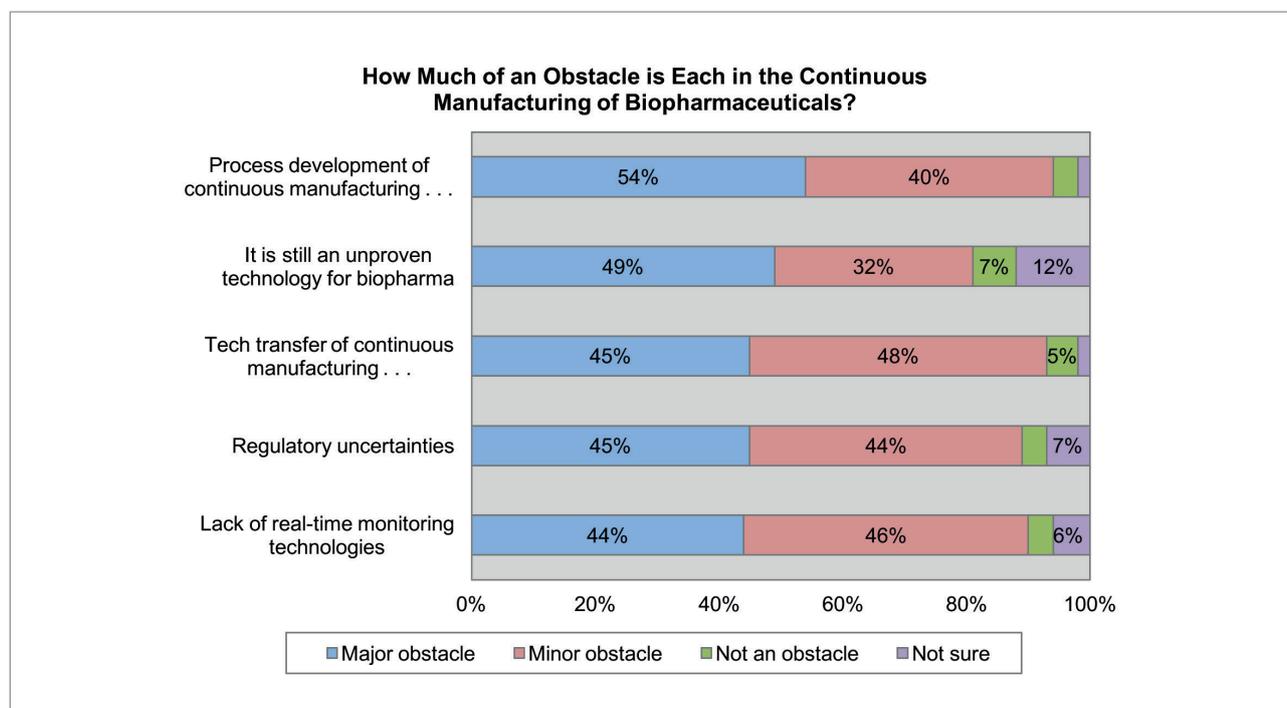
Other major challenges with regard to single-use technologies included supply chain issues, waste disposal, and QA/QC. The table on the following page depicts all of the verbatim responses for this question. These responses are sorted by category or topic.

Other Major Challenges With Regard To Single-Use Technologies

<i>Category</i>	<i>Verbatim Response</i>
Supply chain	Lack of motivation of single use suppliers to collaborate for the benefit of the patient
Supply chain	Over dependence on suppliers for key consumables, e.g. STR bag
Supply chain	Supply chain management
Supply chain	The robustness of the single use components is a major issue. For example, manifolds come in at the incorrect length and cable ties can lead to leaks on sections of line. Depending on the manufacturer of the consumable, the quality can vary.
Supply chain	Vendor diversity
Waste disposal	Disposability.
Waste disposal	Disposing of disposables recycling?... green sustainability?
Waste disposal	Environmental cost, as I think the government is bringing in a tax on single use plastics. Disposal costs.
Waste disposal	Sustainability issues
QA/QC	access to standardized methods of integration
QA/QC	Assurance of sterility
QA/QC	Stability data
IT, data integrity	Lack of standardization - improvement of statistical data analysis and clustering data, for better interpretation of scientific results
Microbial processes	Single use solution for microbial processes
Staff, training	Lack of knowledge, training, experienced individuals
Warehousing	The sheer amount of space you require for the warehousing of all the consumables

RESULTS AND CONCLUSIONS

13. Interest in the continuous manufacturing of biopharmaceuticals is on the rise. How much of an obstacle is each of the following issues?



The attributes in this graph are listed in descending percentage of a “major obstacle” rating. The values in each horizontal bar total 100%. Some bar segments with smaller values are not labeled due to space constraints. Attributes containing an ellipsis have been shortened due to space constraints.

Survey respondents considered most of these challenges to be fairly substantial obstacles in the continuous manufacturing of biopharmaceuticals, with 44% to 54% of the survey respondents rating the following areas as being major obstacles: challenges in the process development of continuous manufacturing processes (54%), still being an unproven technology for biopharma (49%), challenges in the tech transfer of continuous manufacturing processes (45%), regulatory uncertainties (45%), and a lack of real-time monitoring technologies (44%).

Individuals working in biopharma companies were more likely to consider the fact that continuous manufacturing is still an unproven technology for biopharma to be a major obstacle. Those working for contract service providers were more likely to consider challenges in the tech transfer of continuous manufacturing to be a major obstacle. Those working in consulting firms were more likely to consider most of these issues to be major obstacles.

Challenges in the process development of continuous manufacturing processes has been the most often cited major challenge in all three surveys. In contrast, regulatory uncertainties and a lack of real-time monitoring technologies appear to be trending downward in terms of being major challenges. Three-fifths (60%) considered regulatory uncertainties a major challenge in 2016, 49% did so in 2017, and 45% did so in 2018. Fifty-six percent (56%) considered a lack of real-time monitoring technologies a major challenge in 2016, 52% did so in 2017, and 44% did so in 2018.

RESULTS AND CONCLUSIONS

14. If there are other major obstacles with regard to continuous manufacturing that were not listed above, please note them here.

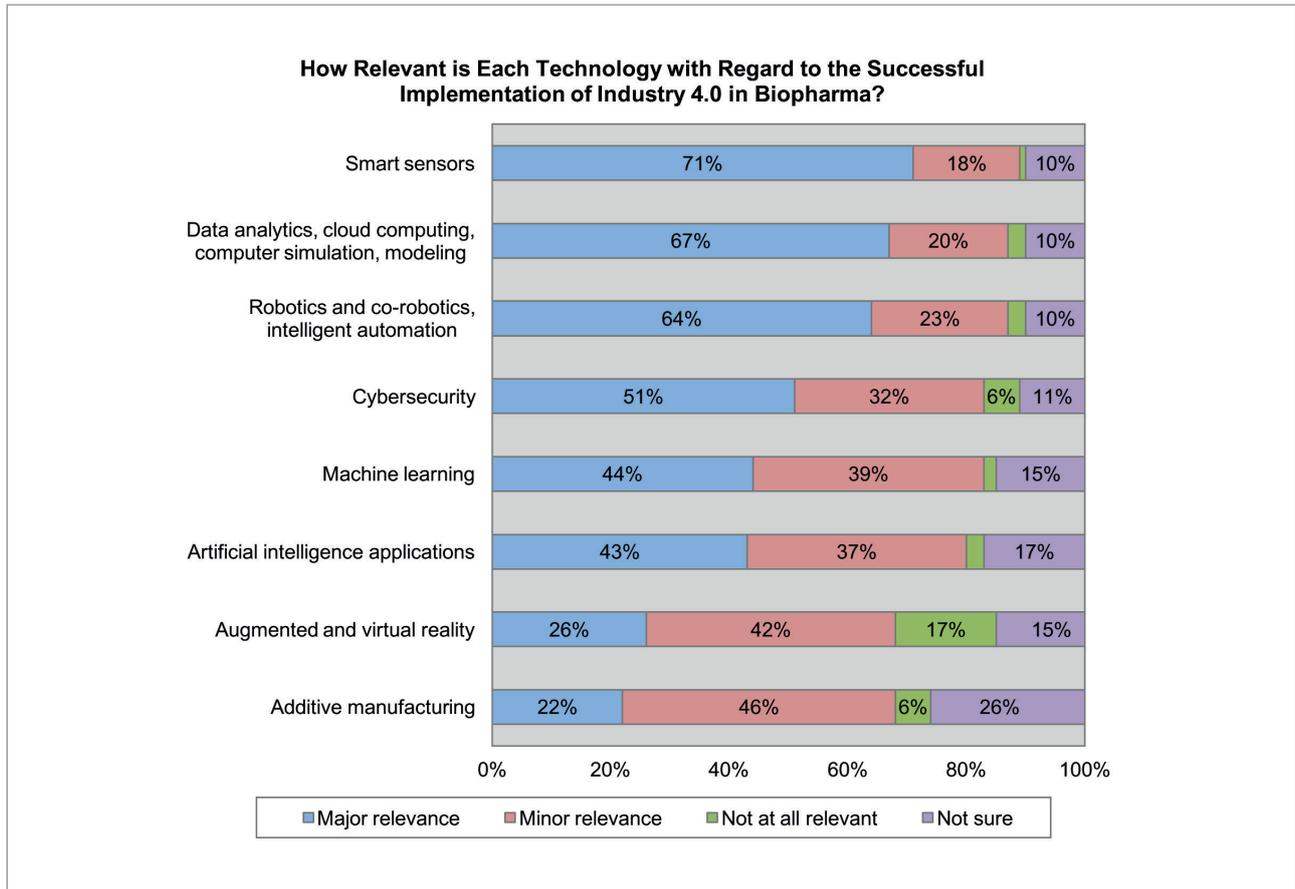
Other major obstacles for continuous manufacturing concerned staff, training and changing the existing infrastructure that is currently in place. The following table depicts all of the verbatim responses for this question. These responses are sorted by category or topic.

Other Major Obstacles With Regard To Continuous Manufacturing

<i>Category</i>	<i>Verbatim Response</i>
Staff, training	Adequate training for the operators
Staff, training	Application of learning from other areas of Biopharma
Staff, training	Every end user is approaching it differently and the ones that look to be the furthest advanced are not sharing best practice. This makes life difficult for contract manufacturers.
Staff, training	Skills and competencies in manufacturing, quality, and regulatory areas
Existing infrastructure	Existence of large amounts of established stainless-steel capacity
Existing infrastructure	Infrastructure
Existing infrastructure	Legacy technologies
Automation	Automation testing
Sterility	Aseptic connections and filling during continuous manufacturing

RESULTS AND CONCLUSIONS

15. How relevant are the following technologies with regard to the successful implementation of Industry 4.0 in biopharma?



The attributes in this graph are listed in descending percentage of a “major relevance” rating. The values in each horizontal bar total 100%. Some bar segments with smaller values are not labeled due to space constraints.

The technologies that were considered to be the most relevant with regard to implementation of Industry 4.0 were smart sensors (71%); data analytics, cloud computing, computer simulation, modeling (67%); and robotics and co-robotics, intelligent automation (64%).

Cybersecurity (51%), machine learning (44%), and artificial intelligence applications (43%) were cited less often. Augmented and virtual reality (26%) and additive manufacturing (22%) were cited least often.

Individuals who were located in Asia, Australia, Pacific Rim were more likely to consider robotics and co-robotics, intelligent automation to be of major relevance while those located in Europe were less likely to do so.

Individuals who worked in consulting firms were more likely to consider smart sensors and robotics/co-robotics, intelligent automation to be of major relevance. Individuals who worked for contract service providers were also more likely to consider robotics/co-robotics, intelligent automation to be of major relevance with regard to the successful implementation of Industry 4.0.

RESULTS AND CONCLUSIONS

This question was first asked in the 2018 survey. In the previous two surveys this question concerned Process Analytical Technologies (PAT).

16. If there are other major technologies that are relevant to the successful implementation of Industry 4.0 that were not listed above, please note them here.

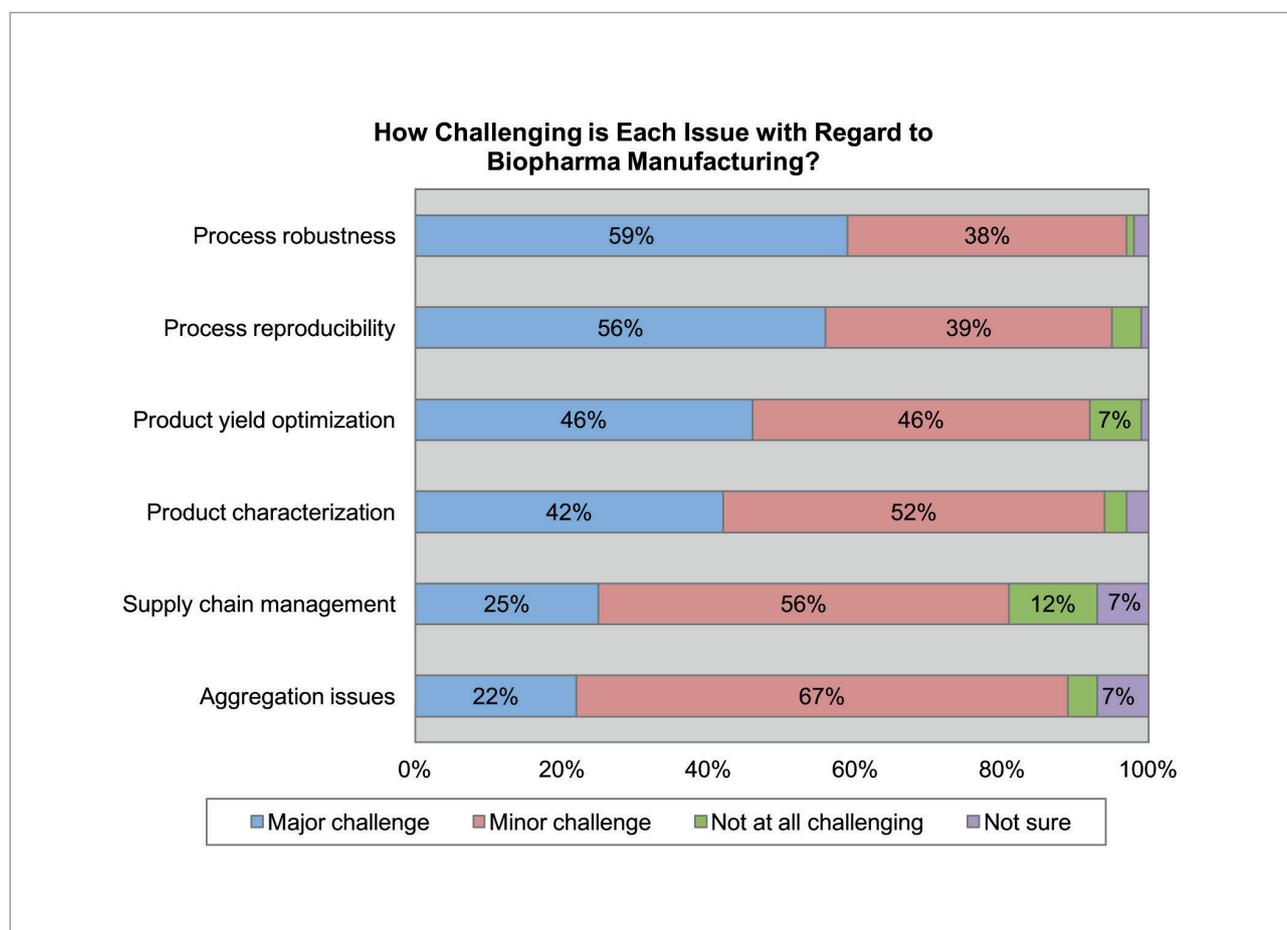
Other major challenges that were considered to be relevant to the successful implementation of Industry 4.0 included regulatory approval and several single mentions. The following table depicts all of the verbatim responses for this question. These responses are sorted by category or topic.

Other Major Obstacles With Regard To Continuous Manufacturing

<i>Category</i>	<i>Verbatim Response</i>
Regulation	Regulations
Regulation	Regulatory change process
Ability to adapt	The will if the industry to adopt as, the IS a major issue in the uptake in certain new technologies... As the saying goes in IT.. "No one gets fired for buying IBM" ... because it has a heritage, and is the leader in the industry... There is a reluctance in accepting new technologies
Automation	Automation testing

RESULTS AND CONCLUSIONS

17. How challenging is each of the following issues regarding biopharma manufacturing?



The attributes in this graph are listed in descending percentage of a “major challenge” rating. The values in each horizontal bar total 100%. Some bar segments with smaller values are not labeled due to space constraints.

The biggest challenges with regard to biopharma manufacturing were process robustness (59% considered this a major challenge) and process reproducibility (56%).

Product yield optimization (46%) and product characterization (42%) were considered to be somewhat less challenging. Supply chain management (25%) and aggregation issues (22%) were considered to be the least challenging issues.

Individuals with 3 or more years of work experience were more likely to consider process robustness to be a major challenge while those with less than 3 years of experience were less likely to do so.

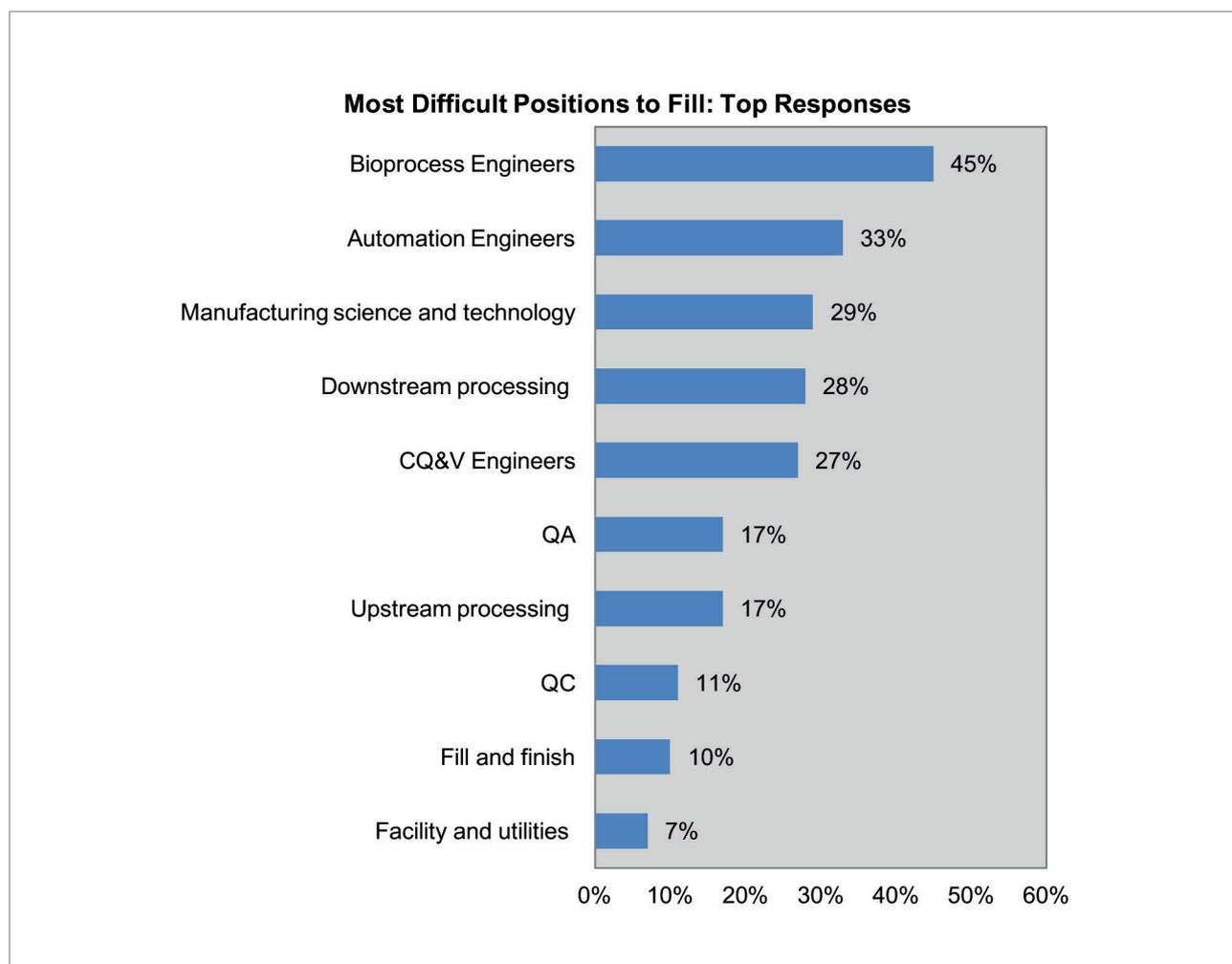
The issues or key challenges faced with regard to biopharma manufacturing have been similar over the last three surveys. One modest change concerns a slight downward trend in the level of challenge for supply chain management: in 2016 34% considered it a major challenge, 28% did so in 2017, and 25% did so in 2018.

RESULTS AND CONCLUSIONS

STAFF DEVELOPMENT

18. Which of the following types of staff are you having the most difficulty hiring? (Select up to five)

The following graph depicts the top responses for this question. A table with all of the responses follows the comments below.



Survey respondents were allowed to choose more than one response to this question; therefore the responses total more than 100%.

A majority (78%) of the survey respondents had difficulty filling one or more positions; the remaining 22% had no issues with hiring staff (10%) or were not sure (12%)—see the table below.

Survey respondents had the most difficulty hiring bioprocess engineers (45%), followed by automation engineers (33%), manufacturing science and technology staff (29%), downstream processing staff (28%), and CQ&V engineers (27%).

RESULTS AND CONCLUSIONS

The remaining types of positions were cited less often: QA (17%), upstream processing (17%), QC (11%), fill and finish (10%), and facility and utilities (7%).

Individuals who worked in biopharma companies were more likely to cite upstream processing while those who worked for contract service providers were more likely to cite bioprocess engineers.

In general, individuals who worked in small companies/start-ups were more likely to have difficulty hiring downstream processing, QA, and QC staff while those who worked in large companies were more likely to have difficulty hiring bioprocess engineers, automation engineers, and facility and utilities staff.

Individuals who worked in organizations with a primary focus on vaccines were more likely to have difficulty hiring bioprocess engineers while those who worked in organizations that were focused on monoclonal antibodies or cell therapies were less likely to do so.

This question was changed in 2017 from one where each position was rated in terms of difficulty in hiring to a multiple-choice question (selecting up to five positions). The difficulty in hiring specialized staff in biopharma manufacturing was similar in 2017 and 2018.

The table below depicts all of the responses for this question.

Most Difficult Positions To Fill

<i>Response</i>	<i>%</i>
Bioprocess Engineers	45%
Automation Engineers	33%
Manufacturing science and technology	29%
Downstream processing	28%
CQ&V Engineers	27%
QA	17%
Upstream processing	17%
QC	11%
Fill and finish	10%
Facility and utilities	7%
Other	10%
Have no issues with hiring staff	10%
Not sure	12%

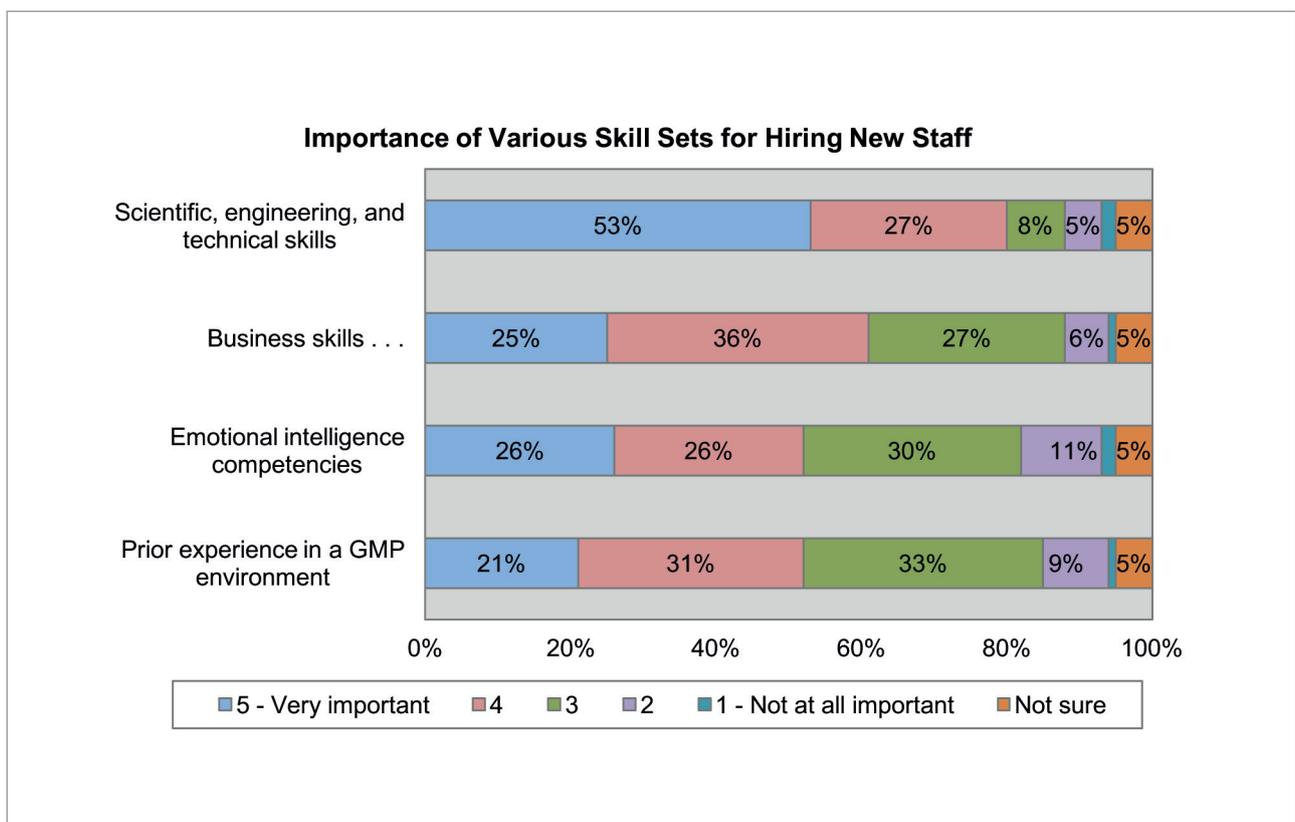
Other fill-in responses (10%) included cleaning validation and process operators.

RESULTS AND CONCLUSIONS

19. With regard to hiring new staff, how important is each of the following skill sets? (Please use a scale from 1 to 5, with 1 being not at all important and 5 being very important.)

The following graph depicts the top responses for this question. A table with all of the responses follows the comments below.

Survey respondents were allowed to choose more than one response to this question; therefore the responses total more than 100%.



The attributes in this graph are listed in descending percentage of a rating of 4 plus 5, with 5 being “very important”. The values in each horizontal bar total 100%. Some bar segments with smaller values are not labeled due to space constraints. Attributes containing an ellipsis have been shortened due to space constraints.

When the top two categories are considered, the most important skill set for new hires was scientific, engineering, and technical skills (rated as 4 or 5 by 80% of the survey respondents). The remaining skill sets were each considered quite important by 52% to 61% of the respondents: business skills, such as communication or team work (61%), emotional intelligence competencies (52%), and prior experience in a GMP environment (52%).

The importance of various skill sets has remained relatively constant over the three years. One exception concerns the importance of business skills, such as communication or team work: 39% considered it to be quite important in 2016, 63% did so in 2017, and 61% did so in 2018.

RESULTS AND CONCLUSIONS

20. If there are other very important skill sets when hiring new staff that were not listed above, please note them here.

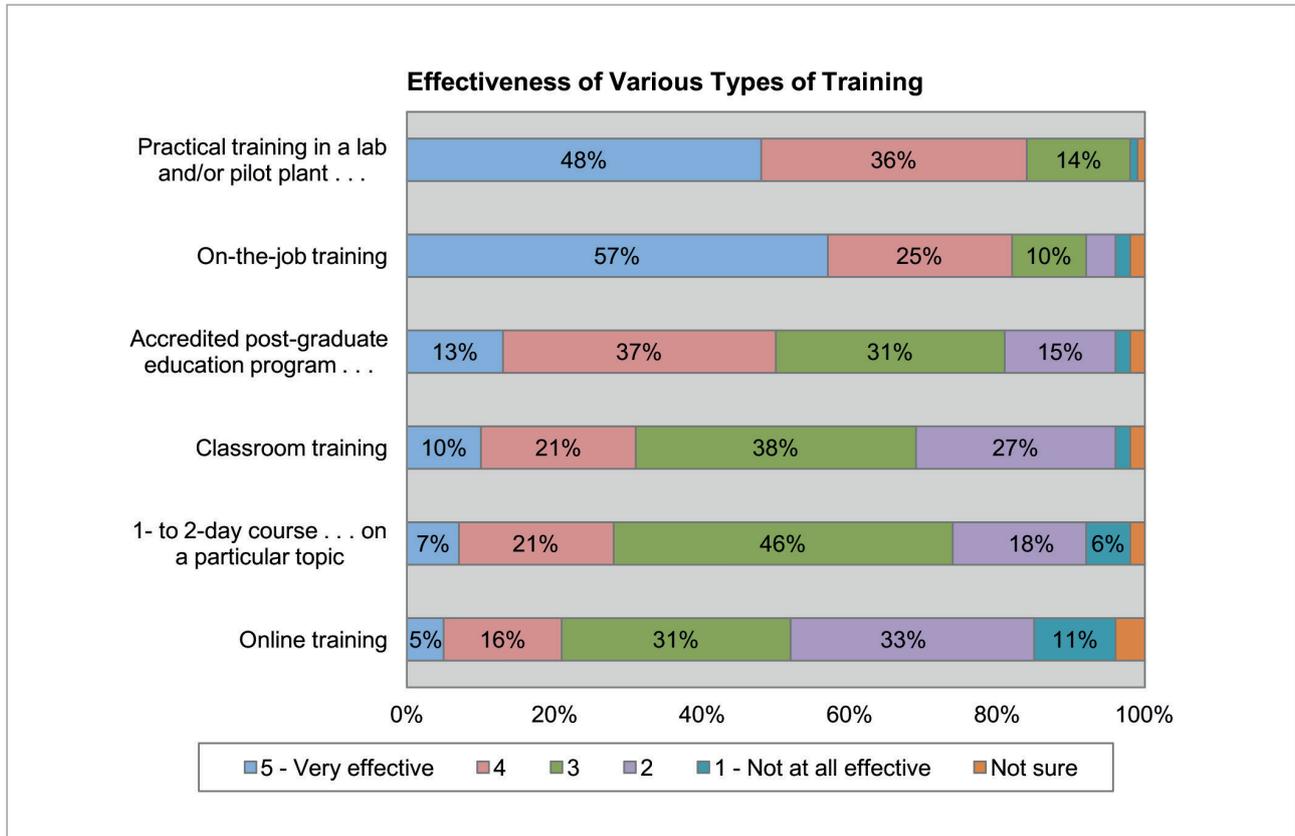
Other very important skill sets for hiring new staff concerned adaptability, honesty and integrity, and several other skills. The following table depicts all of the verbatim responses for this question. These responses are sorted by category or topic.

Other Important Skill Sets For Hiring New Staff

<i>Category</i>	<i>Verbatim Response</i>
Adaptability	Ability to think on feet and think outside the box. Life skills such as being to engage with other and not communicate and not text messages, etc.
Adaptability	Adaptability
Adaptability	Flexibility
Adaptability	inquisitive nature, able to fit with culture, ability to learn
Adaptability	Open to change, new developments and open to give and receive feedback
Honesty, integrity	Honesty
Honesty, integrity	Integrity
Goal oriented	Action driven, willing to see a task through to the end and not walk out when things get difficult. Requires can do mind set and doesn't get discouraged by obstacles.
Goal oriented	Mindset/drive
Leadership skills	Leadership skills
Leadership skills	Management skills

RESULTS AND CONCLUSIONS

21. How effective is each of the following types of training? (Please use a scale from 1 to 5, with 1 being not at all effective and 5 being very effective.)



The attributes in this graph are listed in descending percentage of a rating of 4 plus 5, with 5 being “very effective”. The values in each horizontal bar total 100%. Some bar segments with smaller values are not labeled due to space constraints. Attributes containing an ellipsis have been shortened due to space constraints.

When the top two categories are considered, the most effective types of training were practical training in a lab and/or pilot plant environment (rated as 4 or 5 by 84% of the respondents) and on-the-job training (82%). An accredited post-graduate education program from a higher-level education institute; for example, Master’s in Science program was considered less effective (50%).

Classroom training (31%), a 1- or 2-day course from a third-party provider on a particular topic (28%), and online training (21%) were considered to be the least effective types of training.

Individuals who were located in Asia, Australia, Pacific Rim were more likely to consider an accredited post-graduate education program from a higher-level education institute to be quite effective while those located in Europe were less likely to do so. Individuals located in Asia, Australia, Pacific Rim were also more likely to consider online training to be quite effective, while those in North America were less likely to do so.

RESULTS AND CONCLUSIONS

Individuals who worked in biopharma companies, contract service providers, or consulting firms were more likely to consider practical training in a lab and/or pilot plant environment and on-the-job training to be quite effective while those who worked for suppliers/vendors, in academia, or in government organizations were less likely to do so.

Individuals with 10 or more years of work experience were more likely to consider practical training in a lab and/or pilot plant environment and on-the-job training to be quite effective while those with less than 10 years of experience were less likely to do so.

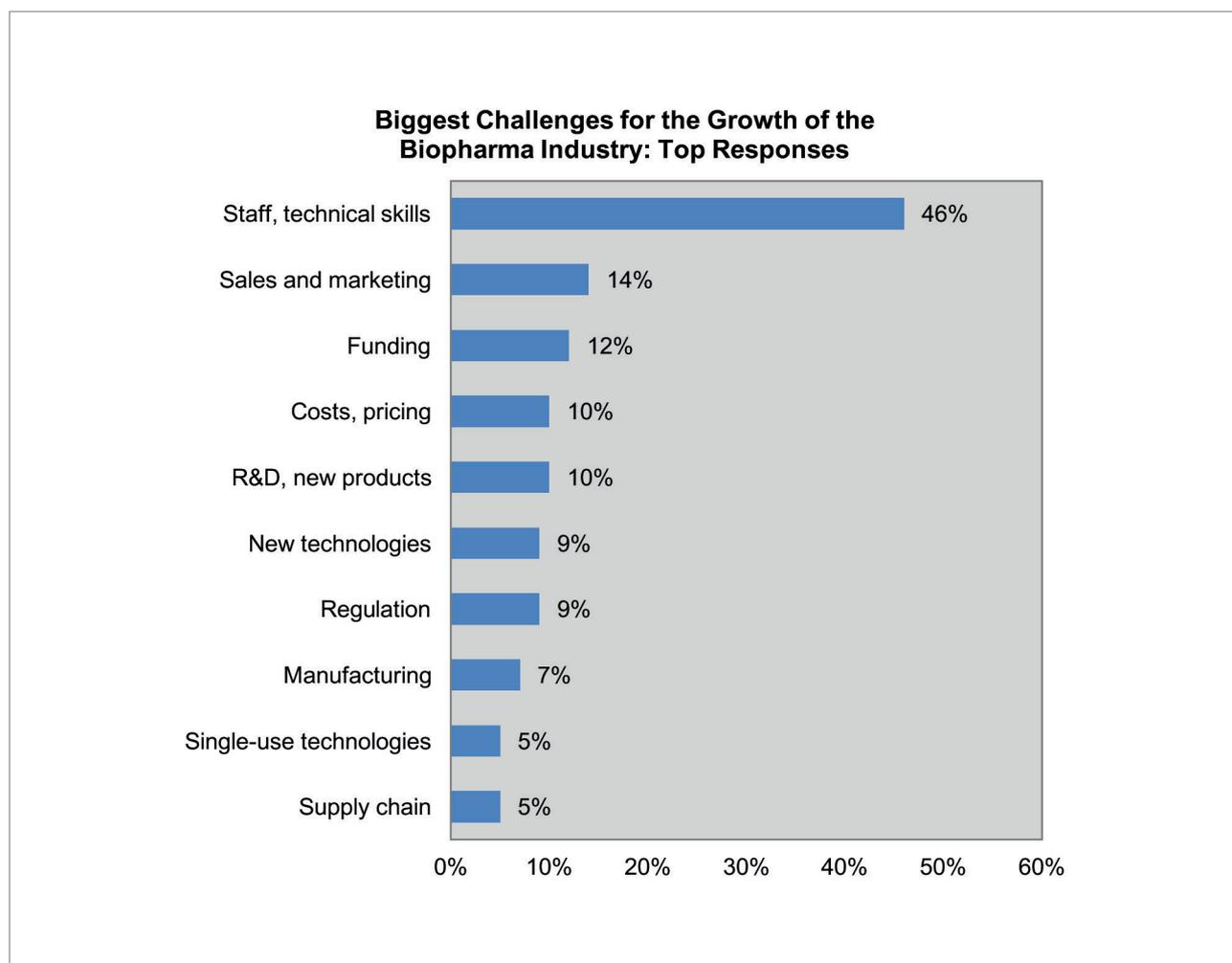
The effectiveness of the various types of training has been similar over the three years.

RESULTS AND CONCLUSIONS

OPPORTUNITIES AND CHALLENGES

22. *What are the biggest challenges for the growth of the biopharma industry?*

The verbatim responses for this question were categorized to produce the following graph which depicts the top responses. A table with all of the types of responses follows the comments below.



Survey respondents were allowed to provide more than one response to this question; therefore the responses total more than 100%.

The biggest challenge for the growth of the biopharma industry concerned staff, technical skills (46%).

Several other types of responses were cited less often: sales and marketing (14%), funding (12%), costs/product pricing (10%), and R&D/new products (10%). The remaining types of responses were each cited by 9% or fewer respondents.

RESULTS AND CONCLUSIONS

Staff, technical skills was considered a major challenge in both the 2017 and 2018 surveys but was cited more often in the 2018 survey (29% cited this as a major challenge in 2017 while 46% did so in 2018). Costs, pricing was considered less of a challenge in 2018 compared to 2017 (29% cited this as a major challenge in 2017 while only 10% did so in 2018).

The following table depicts all of the types of responses for this question.

Biggest Challenges For The Growth Of The Biopharma Industry

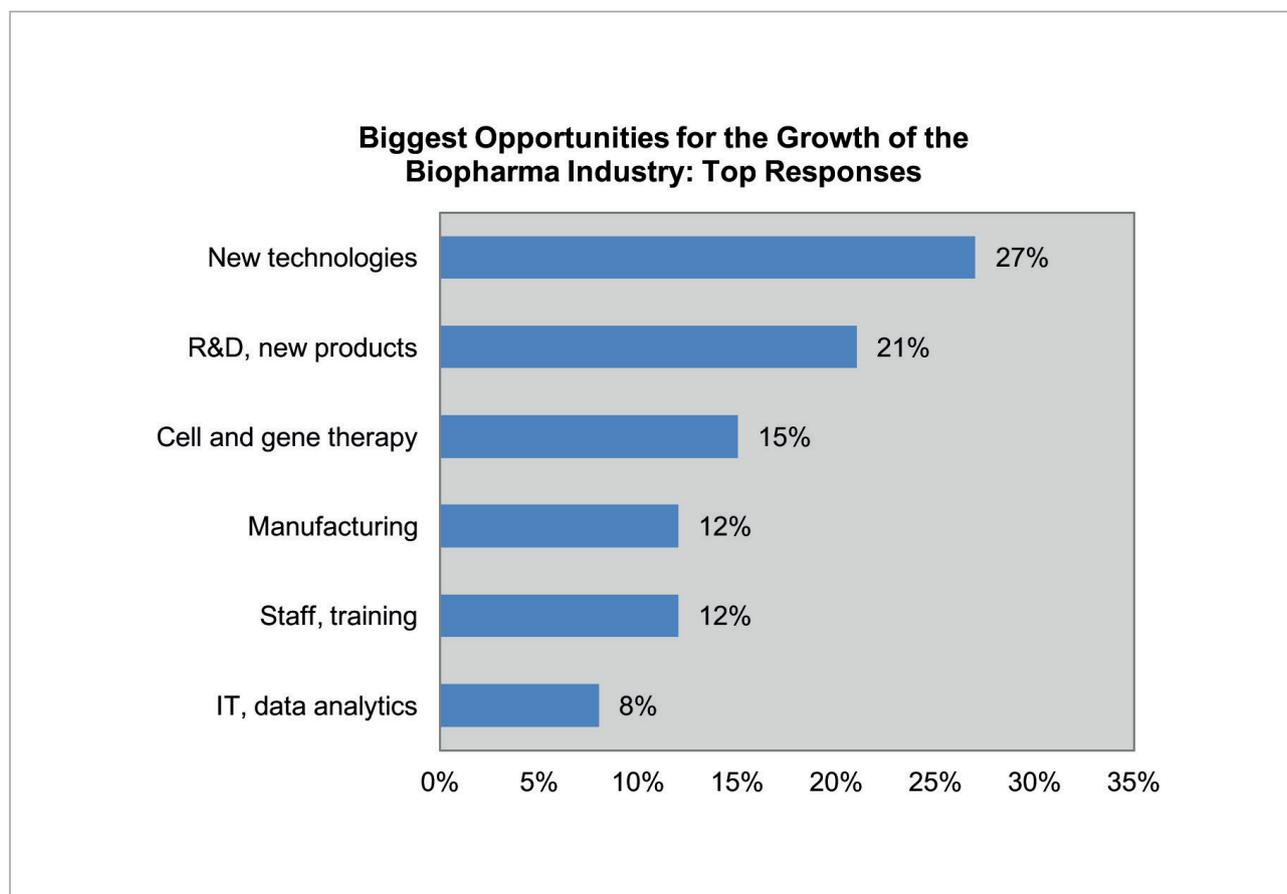
<i>Category</i>	<i>Verbatim Response</i>
Staff, technical skills	46%
Sales and marketing	14%
Funding	12%
Costs, pricing	10%
R&D, new products	10%
New technologies	9%
Regulation	9%
Manufacturing	7%
Single-use technologies	5%
Supply chain	5%
Cell and gene therapy	4%
Geopolitics	4%
IT, data integrity	4%
QA/QC	4%
Reimbursement	4%
Speed to market	4%
Clinical trials	2%
Operations	2%
Outsourcing	2%
Personalized medicine	2%

An Excel file with all of the coded verbatim responses is included separately from this report.

RESULTS AND CONCLUSIONS

23. What are the biggest opportunities for the growth of the biopharma industry?

The verbatim responses for this question were categorized to produce the following graph which depicts the top responses. A table with all of the types of responses follows the comments below. *Survey respondents were allowed to provide more than one response to this question.*



The biggest opportunities for the growth of the biopharma industry concerned new technologies (27%) and R&D, new products (21%).

Other types of responses were cited somewhat less often: cell and gene therapy (15%), manufacturing (12%), staff, training (12%), and IT/data analytics (8%). The remaining types of responses (see the table below) were each cited by 6% or fewer respondents.

New technologies, R&D/new products, and cell and gene therapy were the top three responses for both the 2017 and 2018 survey. New technologies was cited by 16% of the respondents in 2017 and by 27% of the respondents in 2018.

The table on the following page depicts all of the types of responses for this question.

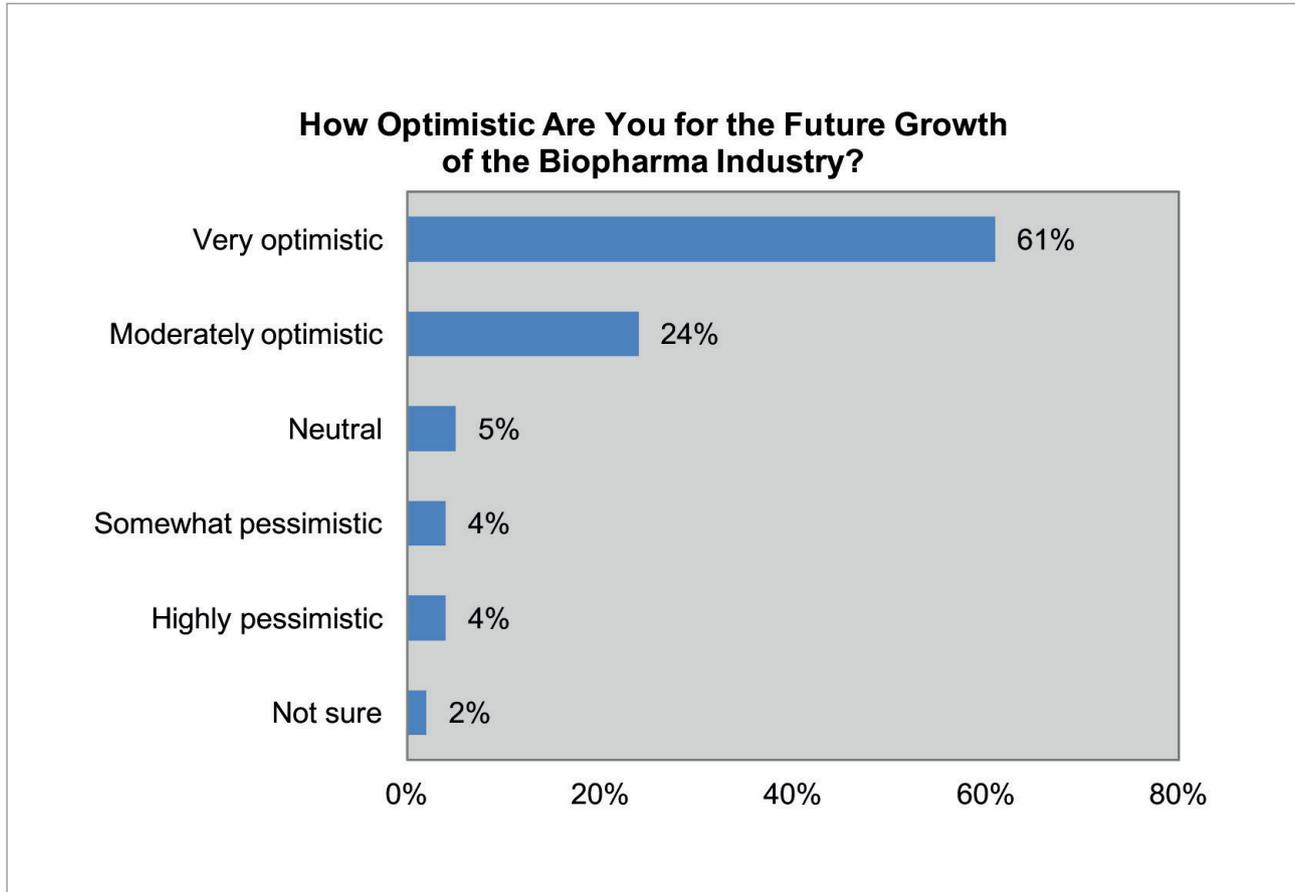
RESULTS AND CONCLUSIONS

Biggest Opportunities For Growth Of The Biopharma Industry

<i>Category</i>	<i>%</i>
New technologies	27%
R&D, new products	21%
Cell and gene therapy	15%
Manufacturing	12%
Staff, training	12%
IT, data analytics	8%
Costs	6%
Funding	6%
Geopolitics	6%
Patient focus	6%
Single-use technologies	6%
Global economy	4%
Ability to adapt	2%
Partnerships	2%
Speed to market	2%

RESULTS AND CONCLUSIONS

24. Overall, how optimistic are you for the future growth of the biopharma industry?



A majority (85%) of the survey respondents were very optimistic (61%) or moderately optimistic (24%) for the future growth of the biopharma industry. Five percent (5%) were neutral and 8% were somewhat pessimistic (4%) or highly pessimistic (4%). The remaining 2% were not sure.

Individuals located in Europe were more likely to be very optimistic or moderately optimistic while those located in Asia were more likely to be neutral, somewhat pessimistic, or highly pessimistic for the future growth of the biopharma industry.

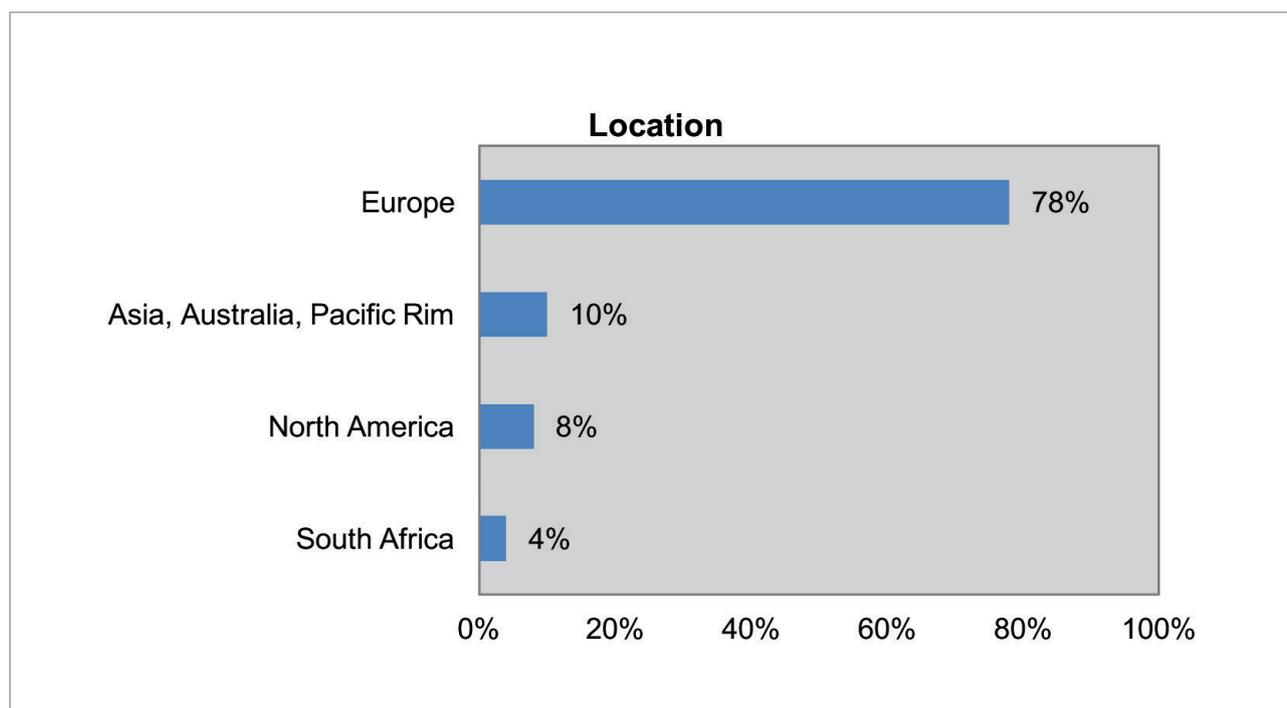
Individuals with 10 or more years of work experience were more likely to be very optimistic while those with less than 3 years of experience were more likely to be neutral or somewhat pessimistic for the future growth of the biopharma industry.

The level of optimism for the future growth of the biopharma industry has changed little over the three surveys.

RESULTS AND CONCLUSIONS

DEMOGRAPHICS

25. *Where are you located?*

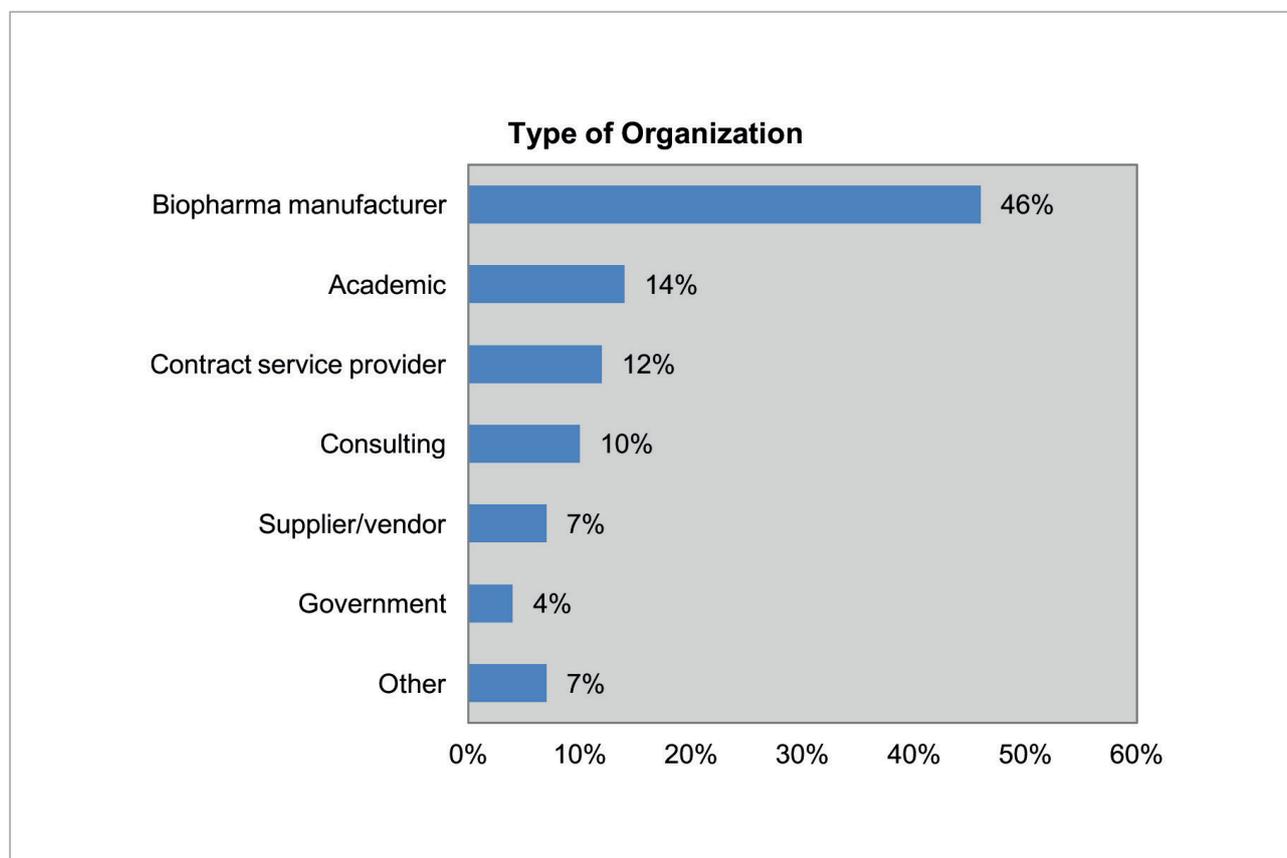


Seventy-eight percent (78%) of the survey respondents were located in Europe; 10% were in Asia, Australia, Pacific Rim; and 8% were in North America. The remaining 4% were located in South Africa.

The location of survey respondents was not tracked in the 2016 survey. In the 2017 survey, there were fewer respondents from Europe and more respondents from North America and Asia, Australia, Pacific Rim. In the 2017 survey, 45% were from Europe, 35% were from North America, and 16% were from Asia, Australia, Pacific Rim).

RESULTS AND CONCLUSIONS

26. In which of the following types of organization do you work or study?
(If more than one applies, please select the one where you spend the most time.)



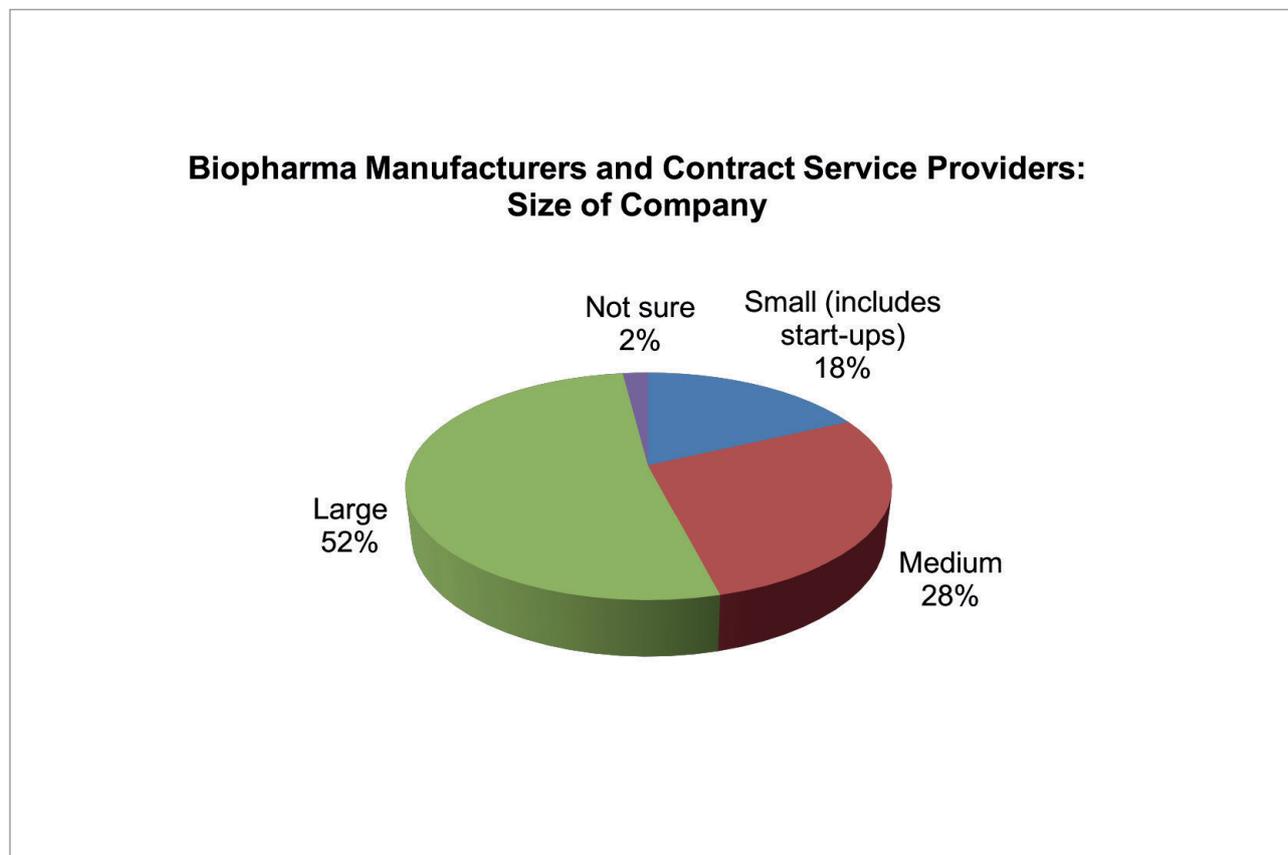
Forty-six percent (46%) of the survey respondents worked for biopharma manufacturers, 12% worked for contract service providers, and 10% were consultants. Fourteen percent (14%) were affiliated with academic institutions, 7% worked for suppliers/vendors, and 4% worked in government organizations.

Other fill-in responses (7%) included engineering firms and publishers.

A much larger percentage of survey respondents in the 2017 and 2018 surveys (46% to 57%) were working in biopharma manufacturing compared to the 2016 survey (38%).

RESULTS AND CONCLUSIONS

27. Which best describes your company?



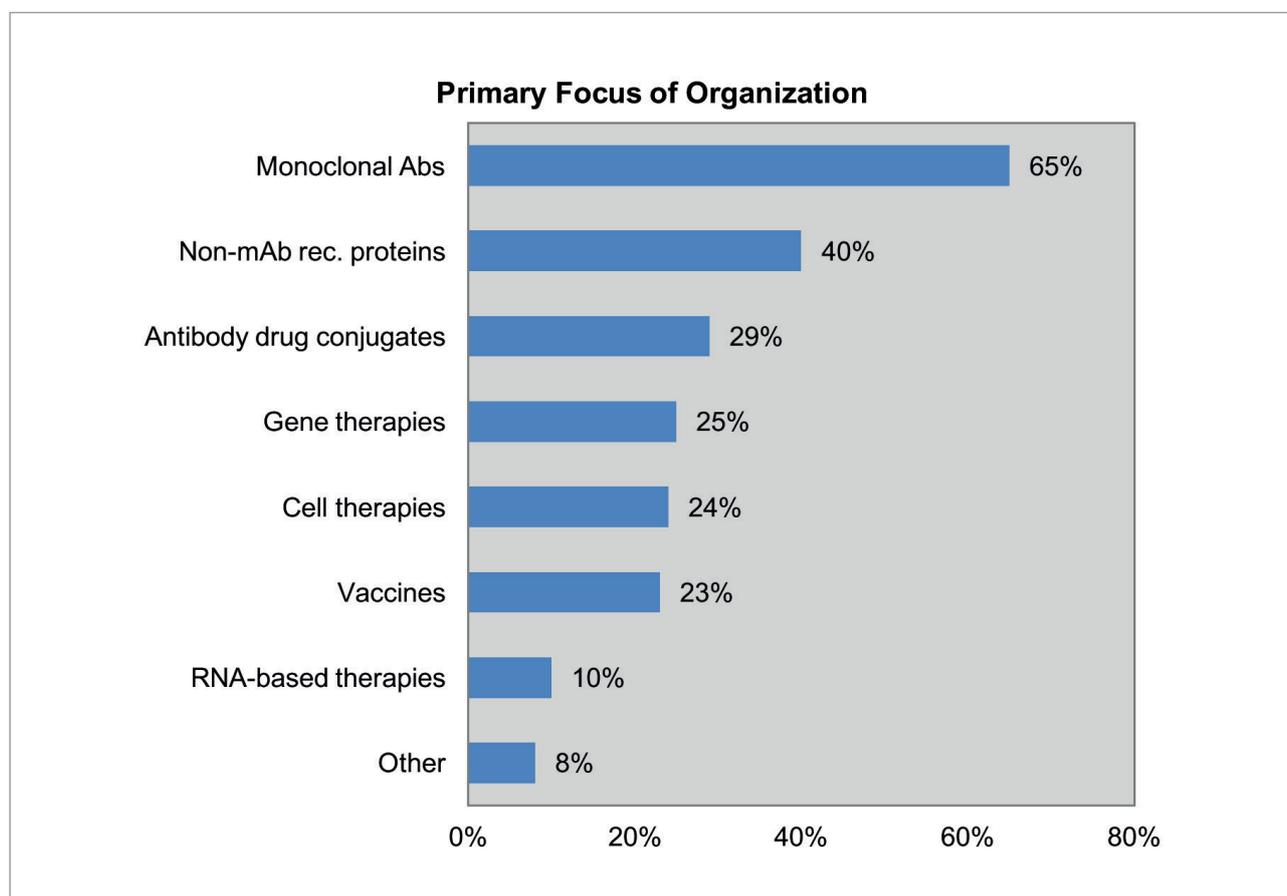
This question was presented to those survey respondents who worked for biopharma manufacturers or contract service providers (from question 30).

One-half (52%) of these industry survey respondents worked in large companies. Twenty-eight percent (28%) worked in medium-size companies. And 18% worked in small companies or start-ups. The remaining 2% were not sure.

This question was not asked in the 2016 survey. The responses from the 2017 and 2018 surveys are similar.

RESULTS AND CONCLUSIONS

28. *What therapies are the primary focus of your organization? (Select all that apply)*



Survey respondents were allowed to provide more than one response to this question; therefore the responses total more than 100%.

On average, each survey respondent cited two areas of primary focus for their organization.

The most common focus for organizations was mAbs (65%), followed by non-mAb recombinant proteins (40%).

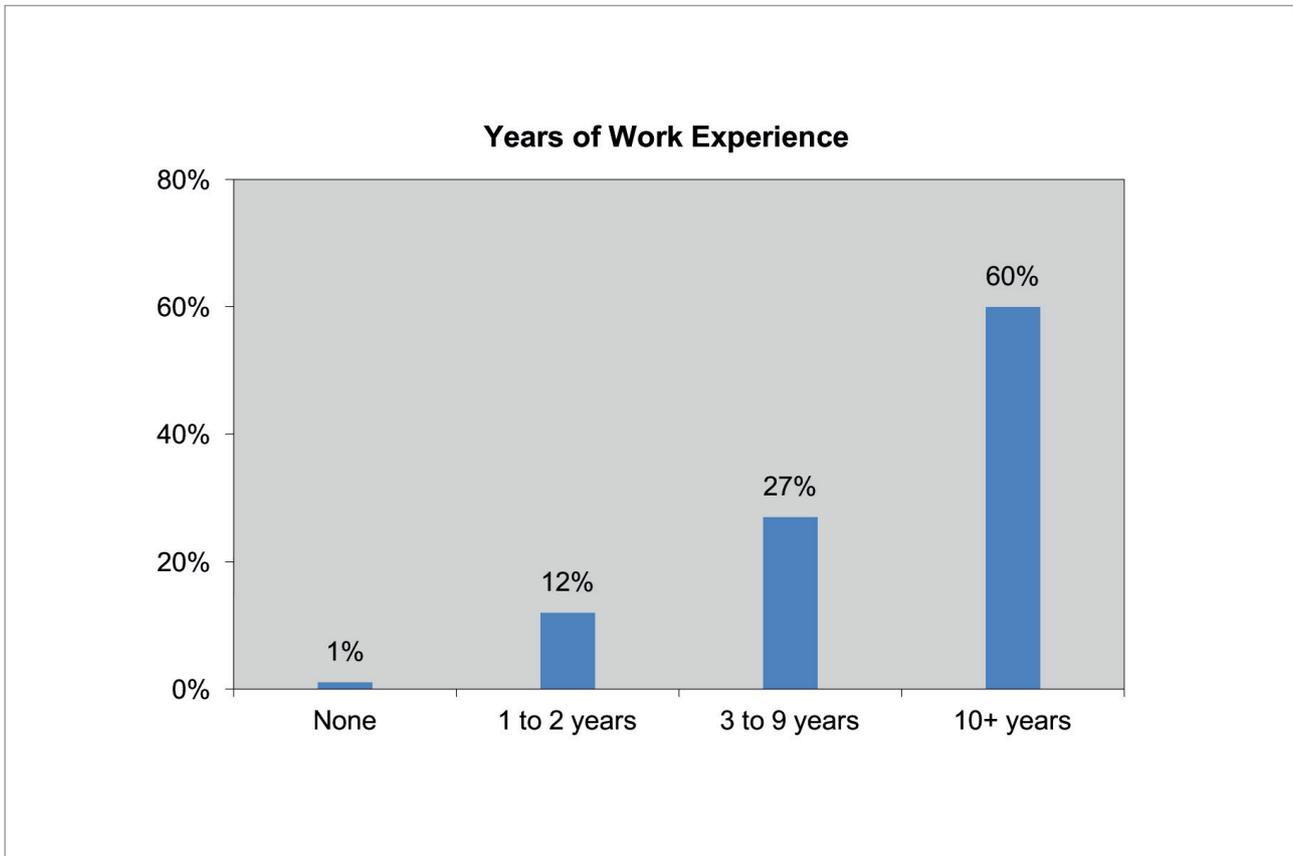
Antibody drug conjugates (29%), gene therapies (25%), cell therapies (24%), and vaccines (23%) were cited less often. RNA-based therapies were a focus for 10% of organizations.

Other fill-in responses (8%) included blood products, insulin, and other diabetic APIs.

This question was first asked in the 2018 survey.

RESULTS AND CONCLUSIONS

29. How many years of work experience do you have?



Three-fifths (60%) of the survey respondents had 10 or more years of work experience. Twenty-seven percent (27%) had 3 to 9 years of work experience and 12% had 1 to 2 years of work experience. The remaining 1% of the respondents had no work experience.

Respondents in the 2016 survey were less experienced: 45% had 10 or more years of work experience in 2016, 65% had 10 or more years of experience in 2017, and 60% had 10 or more years of experience in 2018. Years of work experience was similar for the 2017 and 2018 surveys.

BIOPHARMA

TRENDS