Cytokines and Growth Factors: A Market Study

Executive Summary

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Technology Overview

Cytokines and growth factors include groups of molecules also called interleukins, hematopoietic factors, interferons and chemokines[1]. As functional messengers between cells, cytokines and growth factors participate in the complex regulatory network which control cellular responses. As our understanding of this network deepens, the development of products for cytokine identification, detection, and quantitation has become an important and distinct area for commercialization.

Cytokines and growth factors are studied in a variety of ways and with a wide variety of platforms in both cell free or cell based assays[2]. There are numerous assays to identify and quantitate cytokines and growth factors or their soluble receptors in supernatants, body fluids, or other cell free solutions. These methods are often immunoassays which utilize antibodies specific to cytokines or cytokine receptors[2,3]. The formats and read-out systems used include ELISA techniques, radiometric assays, fluorescence or chemiluminescence based assays and fluorescent or magnetic beads. Genetic techniques like RT-PCR or mRNA profiling are also being used more often. Cell based assays include detection of labeled cytokines or antibodies to detect cell surface receptors. Cell based assays may also include bioassays which measure proliferative responses in factor dependent cell lines. Flow cytometry is ideal for detection of intracellular cytokine measurement, but also serves as the platform for multiplexed bead arrays. Increased use of mRNA profiles, DNA and protein arrays reflect the rapid adoption of multiplexing in the cytokine field. Cytokine and growth factor determination on a single cell basis can be conducted through ELISPOT, intracellular cytoplasmic staining called ICC or mRNA assays. Immunostaining techniques are also used for detection in tissue sections[2]. Cytokine and growth factor related products, therefore, include antibodies, proteins and nucleic acid probes used in a wide variety of applications from the basic research laboratory through the drug discovery process to *in vivo* therapeutic use.

Report Summary

Key Report Components

Technology Overview
A description of the technologies available for identification, detection and quantitation of cytokine and growth factors.

Market Overview
A broad overview of the market for cytokine and growth factor related tools including market size and growth rate, specific areas predicted to grow significantly, how the rise of multiplex bead-based applications is contributing to the market, leading suppliers of cytokine reagent and analysis tools, and key drivers for the commercial expansion of cytokines and growth factors.

Presentation of Survey Findings
Key findings from the Cytokine and Growth Factor Survey completed by 434 scientists currently using cytokine and growth factor related products in their research or work. Included is a three page summary followed by the results of each survey question in graphical and tabular formats. The survey results are divided into two sections – Respondent Profile and Cytokine and Growth Factor Survey Data.

Questionnaire
The complete 24 question survey including single response, multiple choice, rating, and open-end type questions. See page 15 for the survey questions.

Market Overview

In the Life Science research sector, cytokines and growth factor related products are quantitated most often by ELISA based techniques, but also by immunoblotting , ELISPOT and fluorescent techniques developed for intracellular detection of factors by flow cytometry-all these formats utilize antibody probes[3]. From SEC filings of leading companies in the cytokine and growth factor area[4,5], it is estimated that cytokine and growth factor related products represent an estimated $350 million market which has been growing steadily in the 15% range over the last 5 years[4,5]. The recognized leader in the supply of reagents is R&D Systems with an estimated 50-60% of the overall market. Other major competitors include BD Biosciences, Invitrogen, through its Biosource product line, Peprotech, as a supplier of recombinant proteins and Thermo Fisher, through its Endogen business[4].

The worldwide In Vitro Diagnostics (IVD) reagents market is estimated at $35 billion in 2007 and expected to grow to $45 billion by 2010, with an overall CAGR of 7.1%[6,7]. The immunoassay market in 2006 in the U.S. was estimated at $3.2 billion. The U.S. represents approximately 40% of the worldwide market which would be an estimated $7 billion, growing at a CAGR of 7.5%[6]. The worldwide estimate for IVD immunoassays for immune dysfunction and autoimmune diseases is expected to be about $400 million in 2008[7]. Molecular Diagnostics is expected to grow from $2.5 billion to $5 billion from 2005 to 2010, at a CAGR of 15%[8]. In short, the diagnostics area remains a significant opportunity for cytokines and growth factors, although their expanded diagnostic use is dependent on their classification as validated biomarkers or surrogate biodynamic endpoints[9].

The use of multiplexed panels or profiles of cytokines and growth factors has led to increased usage of platforms including mass spectrometry and flow cytometry in addition to plate and chip array readers[10]. One of the fast growing applications for cytokine and growth factor quantitation is the multiplexed bead array using a multispectral set of fluorescent beads - each bead specific for a given factor. This flow cytometry application pioneered by Luminex Corporation has grown into a significant product area estimated to be $160-170 million in 2007. Cytokines and growth factor related products in the multiplexed bead array market may represent approximately 60-70% of product revenues[5]. Bio-Rad, Millipore, Invitrogen, R&D Systems, One Lambda, Thermo Fisher (all Luminex partners) BD Biosciences and others all compete in this rapidly developing area. Based on the possibility of simultaneous high throughput profiling, amenable to protein and nucleic acid quantitation, the platform has also attracted major diagnostic players including Abbott, PerkinElmer, Bayer and Bio-Rad. As Luminex partners[5] all are planning or have developed diagnostics using the bead array technology.

Market Overview (cont'd.)

Cytokine and growth factor related revenues account for 20% of the total world biopharma revenues or $80-100 billion[11]. Approximately 50% of growth factor revenues are for recombinant protein therapies, $15 billion for vaccines, $10 billion for plasma derived proteins and another $5 billion for other modifications or biosimilars of existing recombinant products. Recognition of the integral involvement of pro-inflammatory cytokines like TNF-alpha in the evolution and maintenance of autoimmune disease states such as rheumatoid arthritis, has led to the development of blocking or TNF-alpha inhibitors, now a distinct class of "block-buster "drugs. These drugs mitigate the TNF-alpha driven inflammatory process in rheumatoid arthritis and other inflammatory diseases. Three TNF-alpha inhibitors alone from Amgen, Johnson & Johnson and Abbott accounted for $7 billion in 2006 and the entire anti-TNF-alpha and biological reagents market for rheumatoid arthritis is expected to surpass $10 billion in 2015[12]. According to CHI Insight Pharma reports[13], the biggest single market for growth factors may be anemia, where recombinant erythropoietin drugs have already surpassed sales of $10 billion in 2005.

Another major use for cytokines and growth factors is in the area of cell therapy and regenerative medicine. Regenerative medicine provides the possibility and promise of replacing damaged or diseased cells or tissues through the use of stem cells which are driven to differentiate into specific cell or tissue types prior to direct transfer into recipients. Currently, peripheral blood stem cells are often used for transplants. To enhance the number of circulating stem cells, donors are treated with G-CSF to enhance stem cell mobilization from the bone marrow and increase peripheral stem cell numbers[14]. Estimates for the entire market for stem cell, cytokine and growth factor therapies used in treatment of immunologic or hematologic disorders, is estimated to grow to over $20 billion in 2010[15] from $12.7 billion in 2005, an estimated growth rate of over 10%[15]. Cytokines and growth factors are used not only for *in vivo* expansion of target effector cell populations, but also for *in vitro* expansion and proliferation of specific effector cell populations. The market for supplements and growth factors, which figure strongly in effector cell expansion applications, was estimated at $75 million in 2005 in the U.S. alone, and represented about 10% of the overall select culture media revenues. The CAGR for the U.S. cell culture market is estimated at 8% from 2005 to 2012[16].

Overall, increased utility, adoption of different applications and subsequent commercial expansion of cytokines and growth factors is expected in research, diagnostics and biopharmaceutical sectors. As more cytokines and growth factors become validated biomarkers and are transferred to diagnostic platforms, attractive opportunities are available for research reagent suppliers, such as those indicated in the following survey. Certainly the current market for cytokine and growth factor based drugs is already large - in the $80-100 billion range and is expected to continue rapid growth.

Market Overview (cont'd.)

In summary, there are several key drivers for cytokine and growth factors which will drive commercial expansion. These include:

- In-depth understanding of growth factors and their activities in biological areas of current focus such as neurobiology, cell signaling, angiogenesis and stem cell biology
- Multiplexing and profiling cytokines and growth factors will lead to their validation as biomarkers
- Development of cytokine and growth factor based diagnostics following their validation as biomarkers
- Continued expansion and adoption of cell therapy will drive greater use of cytokines and growth factors as therapeutics or for their use in expansion of effector cell populations

Survey Introduction and Methodology

The 2007 Cytokine and Growth Factor Survey consisted of 24 questions. The questionnaire included single answer, multiple-choice and open-end question types. Demographic information was collected from the following five questions: Country/Region, Institution Type, Job Title, Research Areas, and Highest Degree Earned. A question on the frequency of cytokine and growth factor usage allowed only respondents who currently use cytokines or growth factors at least once a month to participate in the survey. Other respondents were screened out of the survey.

Incentives included a gift certificate for the first 200 participants to complete the survey and an entry into a sweepstakes drawing. The survey was administered online from November 5th to November 16th, 2007 and the data tabulated and presented here.

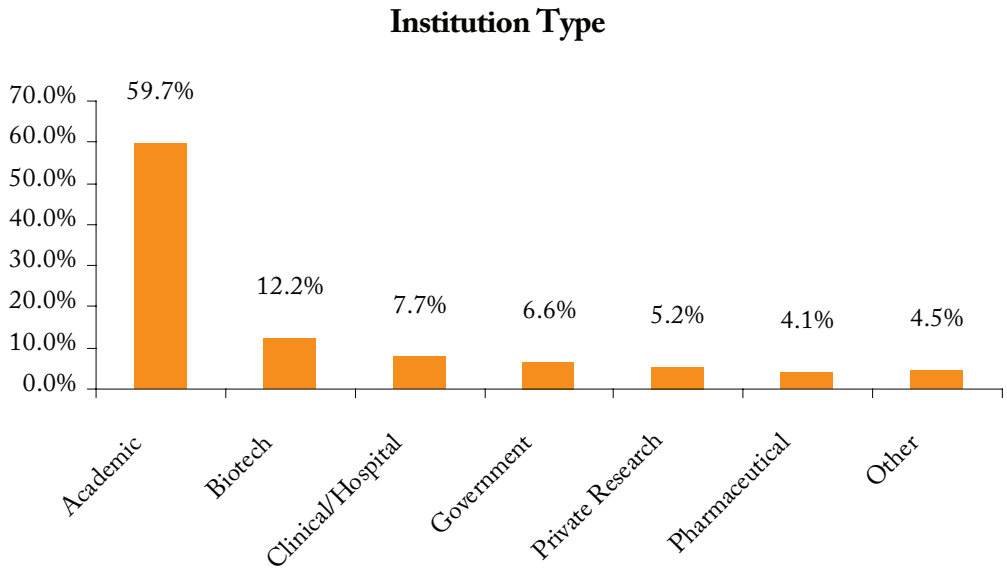
Respondent Profile

What is your institution type?

60% of the respondents are from academia; 16% are from Pharma or Biotech.

N = 558

Institution Type	Count	%
Academic	333	59.7%
Biotech	68	12.2%
Pharmaceutical	23	4.1%
Government	37	6.6%
Private Research	29	5.2%
Clinical/Hospital	43	7.7%
Other (Please specify)	25	4.5%



Which title best applies?

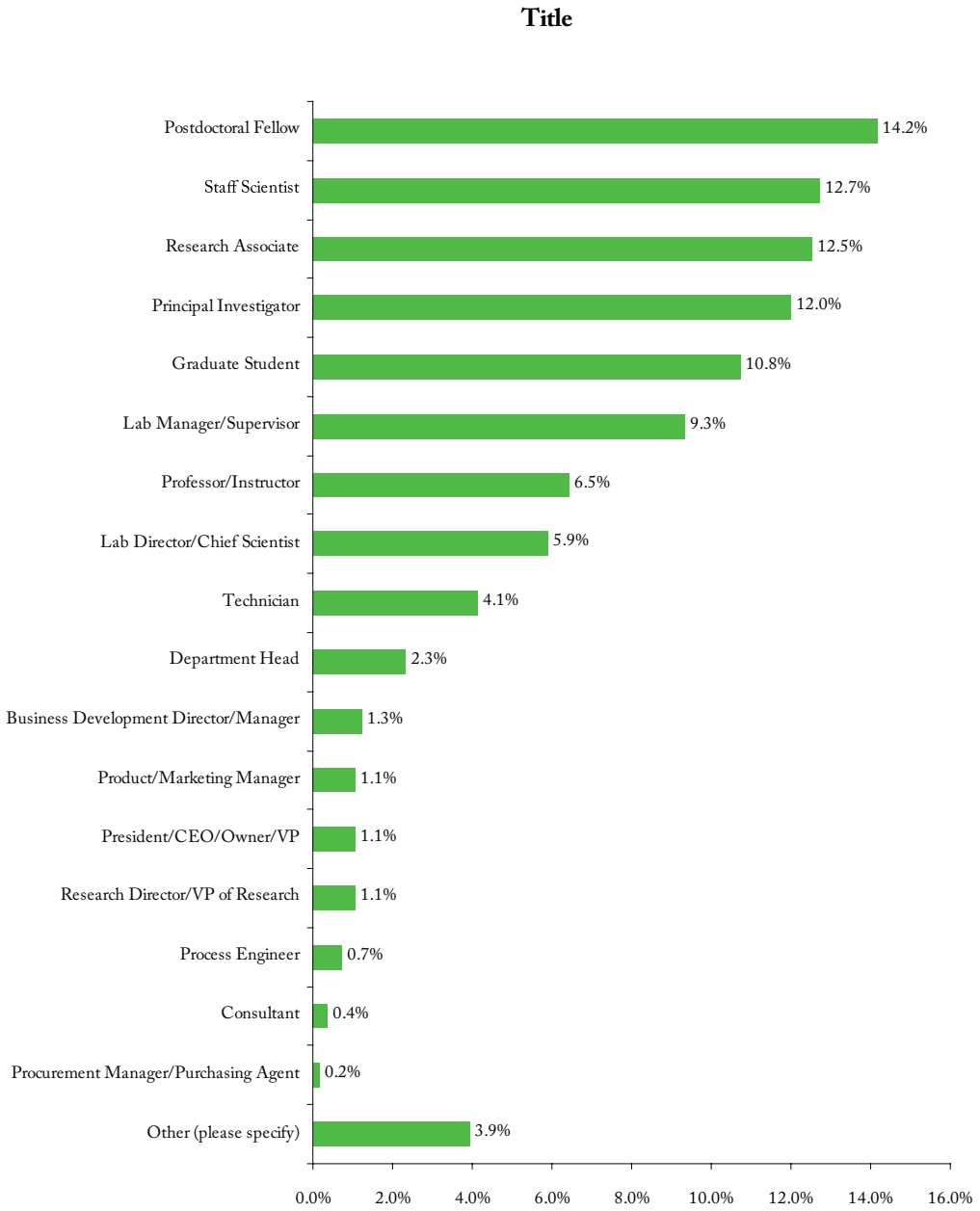
Over 75% of the respondents work at the lab bench.*

N = 558

Title	Count	%
Postdoctoral Fellow	79	14.2%
Staff Scientist	71	12.7%
Research Associate	70	12.5%
Principal Investigator	67	12.0%
Graduate Student	60	10.8%
Lab Manager/Supervisor	52	9.3%
Professor/Instructor	36	6.5%
Lab Director/Chief Scientist	33	5.9%
Technician	23	4.1%
Department Head	13	2.3%
Business Development Director/Manager	7	1.3%
Research Director/VP of Research	6	1.1%
President/CEO/Owner/VP	6	1.1%
Product/Marketing Manager	6	1.1%
Process Engineer	4	0.4%
Consultant	2	0.4%
Other (Please specify)	23	4.1%

*Includes: Postdoctoral Fellow, Staff Scientist, Research Associate, Principal Investigator, Graduate Student, Lab Manager/Supervisor, Technician.

Which title best applies?



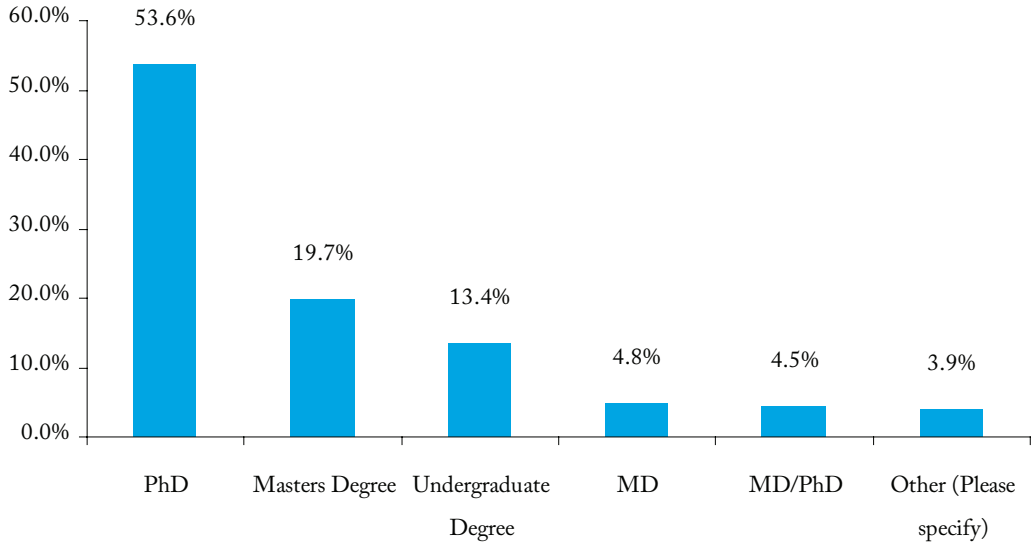
What is your highest professional degree?

Over 58% of the respondents earned a Ph.D. or MD/Ph.D.

N = 558

Degree	Count	%
Ph.D.	299	53.6%
Masters Degree	110	19.7%
Undergraduate Degree	75	13.4%
MD	27	4.8%
MD/Ph.D.	25	4.5%
Other (Please specify)	22	3.9%

Highest Professional Degree



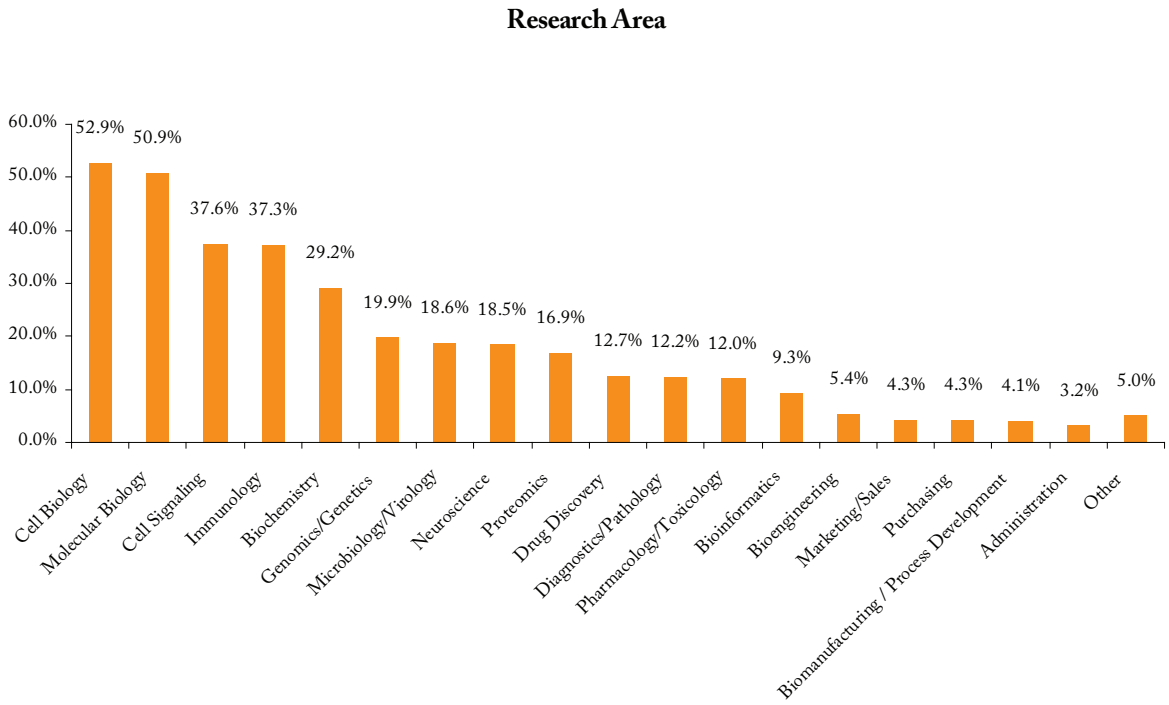
Which of the following are your key areas of research or work? (check all that apply)

Over half of the participants, 53% and 51%, indicate Cell Biology or Molecular Biology as their key research area.

N = 558

Research Area or Work	Count	%
Cell Biology	295	52.9%
Molecular Biology	284	50.9%
Cell Signaling	210	37.6%
Immunology	208	37.3%
Biochemsitry	163	29.2%
Genomics/Genetics	111	19.9%
Microbiology/Virology	104	18.6%
Neuroscience	103	18.5%
Proteomics	94	16.9%
Drug Discovery	71	12.7%
Diagnostics/Pathology	68	12.2%
Pharmacology/Toxicology	67	12.0%
Bioinformatics	52	9.3%
Bioengineering	30	5.4%
Marketing/Sales	24	4.3%
Purchasing	24	4.3%
Biomanufacturing/Process Development	23	4.1%
Administration	18	3.2%
Other (Please specify)	28	5.0%

Which of the following are your key areas of research or work? (check all that apply)

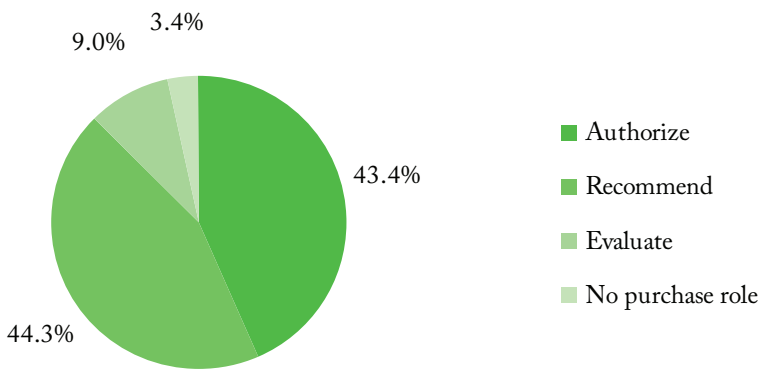


Which best describes your purchasing authority?

88% of the survey audience either authorize or recommend purchases.

N = 558

Purchasing Authority	Count	%
Authorize	242	43.4%
Recommend	247	44.3%
Evaluate	50	9.0%
No purchase role	19	3.4%



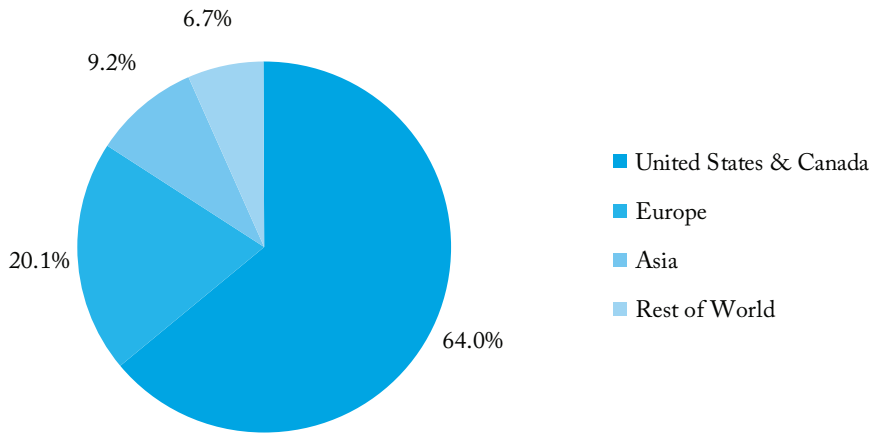
Country

64% of respondents are from the U.S. and Canada; 20% are from Europe; and nearly 10% are from Asia.

N = 433

Country/Region	Count	%
United States and Canada	277	64.0%
Europe	87	20.1%
Asia	40	9.2%
Rest of World	29	6.7%

Country/Region



Appendix: Questionnaire

Cytokine and Growth Factor Survey

1. How often do you use cytokines, growth factors, and related products (e.g. assay kits, antibodies, other assay types) in your research or work?

- Daily
- A few times a week
- Once a week
- A few times a month
- Once a month
- Less than once a month – *"Screened out of the survey"*

2. What is the goal of your research with cytokines or growth factors?

- Basic research
- Disease research
- Drug screening
- Vaccine development
- Others (Please specify)

3. Which cytokines or growth factor families are you currently studying or work with? (Select all that apply)
Please specify the molecule name (i.e. IL2, IL4, etc) in the box provided.

Family/Type	Please type in the cytokine name(s)
Interferons	
Interleukins	
Chemokines	
Transforming growth factors (TGF)	
Epidermal growth factors (EGF)	
Platelet-derived growth factors (PDGF)	
Erythropoietin	
Insulin-Like Growth Factor (IGF)	
Fibroblast Growth Factor (FGF)	
Tumor necrosis factors (TNF)	
Colony stimulating factors (CSF)	
Angiogenen	
Endothelin	
Eph	
LIF/OSM	

Family/Type	Please type in the cytokine name(s)
MDK/PTN	
MIF	
NGF, BDNF, NTF	
NRG	
PEDF	
Thrombopoetin	
VEGF	
Other (please specify)	

4. Which of the following techniques do you currently use or plan to use for measuring cytokine activity? (Select all that apply)

	Currently Use	Plan to Use
Western blot		
ELISA		
ELISPOT		
Flow cytometry		
Mulitplex assays		
Nucleic acid-based techniques (e.g. RT-PCR, DNA Microarray)		
Other (Please specify)		
Do not measure cytokine activity		

5. Have you adopted any new technologies within the last year or plan to adopt new technologies within the next year for cytokine analysis? If yes, please describe what they are.

- Yes (Please describe) _____
- No

6. What supplier comes to mind when you think of cytokine-related research products? ***(open-ended)***

7. What sample type(s) do you primarily use? (Select all that apply)

- Cell culture supernatant
- Serum
- Plasma
- Cell lysate
- Other (Please specify)

8. What cytokine species do you primarily work with? (Select all that apply)

- Human
- Mouse
- Rat
- Non-human primate
- Other (please specify)

9. How much do you typically spend on cytokines, growth factors, and related analysis tools each month?

- Less than $100
- $100 to $500
- $500 to $1000
- $1000 to $2500
- $2500 to $5000
- More than $5000 per month

10. How do you expect this amount to change over the next 12 months?

- Increase by > 50%
- Increase by 25% - 50%
- Increase by 10 – 25%
- Increase by 1% - 10%
- No change
- Decrease by 1% - 10%
- Decrease by 10% - 25%
- Decrease by 25% - 50%
- Decrease by > 50%

11. From which suppliers do you purchase cytokines, growth factors, and assay products? (Select all that apply)

Supplier	Cytokines/Growth Factor/Receptor Recombinant Proteins	Assays and Other Analysis Products
AbD Serotec		
Affinity Bioreagents (ABR)		
ALPCO Diagnostics		
Antigenix America		
Apollo Cytokine Research		
BD Biosciences Pharmingen		
Bio-Rad		
BioVision		

Supplier	Cytokines/Growth Factor/Receptor Recombinant Proteins	Assays and Other Analysis Products
Calbiochem/Novagen		
Cell Signaling Technology		
GE Healthcare (formerly Amersham Biosciences)		
Invitrogen (BioSource International)		
MBL International		
Millipore (CHEMICON/Upstate/Linco)		
PBL Interferon Source		
Peprotech		
Pierce/Endogen (Thermo Fisher Scientific)		
R&D Systems		
Sigma-Aldrich		
Stratagene		
Vision Biosystems		
Other (Please specify)		

12. How important are the following service and support characteristics to you in a supplier of cytokines/growth factors or related products?
1 = Very important
2
3
4 = Neutral
5
6
7 = Not at all important

- Product regularly in-stock (not backordered)
- Knowledgeable technical support
- Ability to purchase products online
- Colleague recommendation
- Supplier reputation
- Useful resources (e.g. protocols, application notes, FAQs) on their website

13. How important are the following service and support characteristics to you in a supplier of cytokines/growth factors or related products?
1 = Very important
2
3
4 = Neutral
5
6
7 = Not at all important

- Sensitivity
- Short assay time
- Wide dynamic range
- Small amount of sample required
- Biological activity
- Good value
- Protein purity
- Specificity
- Stability of protein through multiple freeze/thaw
- High signal-to-noise ratio

14. How would you rate the cytokine suppliers you selected on these product and service characteristics? ***(Only the selected suppliers will appear)***

Supplier	Product Quality	Value	Technical Support	Usefulness of Website
AbD Serotec				
Affinity Bioreagents (ABR)				
ALPCO Diagnostics				
Antigenix America				
Apollo Cytokine Research				
BD Biosciences Pharmingen				
Bio-Rad				
BioVision				
Calbiochem/Novagen				
Cell Signaling Technology				
GE Healthcare (formerly Amersham Biosciences)				
Invitrogen (BioSource International)				
MBL International				
Millipore (CHEMICON/Upstate/ Linco)				
PBL Interferon Source				
Peprotech				

Supplier	Product Quality	Value	Technical Support	Usefulness of Website
Pierce/Endogen (Thermo Fisher Scientific)				
R&D Systems				
Sigma-Aldrich				
Stratagene				
Vision Biosystems				
Other (Please specify)				

Drop down list:
Excellent
Very good
Average
Fair
Poor
Don't know/unaware

15. Would you recommend the following companies to a colleague or friend?
(Only the selected suppliers will appear)
- Yes
- No
- I don't know

16. Are there any cytokines or growth factors you are studying for which you cannot find a supplier?
- Yes
- No

17. If Yes, please list those cytokines or growth factors for which you cannot find a supplier.
(open-ended)

18. Which of the following would you identify as the biggest problems/limitations with your cytokine-based experiments? (Select all that apply)
- Limited availability of recombinant cytokines/growth factors
- Limited availability of cytokine/growth factor assay kits
- Limited amount of sample
- Assay sensitivity
- Resources (i.e. money)
- Time to conduct assays/analysis

19. Please provide any suggestions on how suppliers can improve the cytokine-related products they provide. ***(open-ended)***

Demographic Questions

20. In which type of institution do you work?

- Academic
- Pharmaceutical
- Private Research
- Other (Please specify)
- Biotechnology
- Government
- Clinical/Hospital

21. Which title best applies?

- Professor/Instructor
- Lab Manager/Supervisor
- Business Development Director/Manager
- Department Head
- Account Manager
- Staff Scientist
- President/CEO/Owner/VP
- Postdoctoral Fellow
- Consultant
- Product Manager
- Process Engineer
- Research Associate
- Research Director/VP of Research
- Technician/Research Assistant
- Graduate Student
- Principal Investigator
- Lab Director/Chief Scientist
- Procurement Manager
- Other

22. Which of the following are your key areas of research or work?

- Bioinformatics
- Genomics/Genetics
- Drug Discovery
- Marketing/Sales
- Bioengineering
- Biomanufacturing /Process Development
- Microbiology/Virology
- Cell Biology
- Administration
- Pharmacology/Toxicology
- Neuroscience
- Purchasing
- Cell Signaling
- Immunology
- Diagnostics/Pathology
- Biochemistry
- Molecular Biology
- Proteomics
- Other

23. Which best describes your purchasing authority?

- Authorize
- Recommend
- Evaluate
- No Purchase Role

24. What is your highest professional degree?

- Ph.D.
- Masters Degree
- MD
- MD/Ph.D.
- Undergraduate Degree
- Other (Please specify)