The 2021 WCG Avoca State of the Industry Report

Diversity in Clinical Research Execution and Participation

March 2022

Introduction

- The events of the last two years have created an urgent and nonnegotiable imperative to increase diversity in clinical research: diversity in how such studies are executed and in the types of patients recruited. Moving forward, the industry must contend with fully building diversity into the clinical operations culture; deciding how much executional diversity to maintain and supporting sites in its maintenance; and determining how we can sustainably maintain diversity in the patients involved in clinical research. The 2021 WCG Avoca Industry Survey explored these questions by requesting respondents' candid views regarding the relative priority and drivers of patient diversity in clinical research participation, as well as with their experiences with diversity in clinical research execution.
- The 2021 WCG Avoca Industry Survey was conducted between September and December of 2021.
- Invitations to participate were sent to contacts in WCG Avoca's database. The survey was also discussed during the 2021 WCG Avoca Quality & Innovation Summit with an open invitation to participate, and the link for the survey was posted on the WCG Avoca website and on LinkedIn.

Usage Guidelines

Characteristics of the Sample

Participating Companies

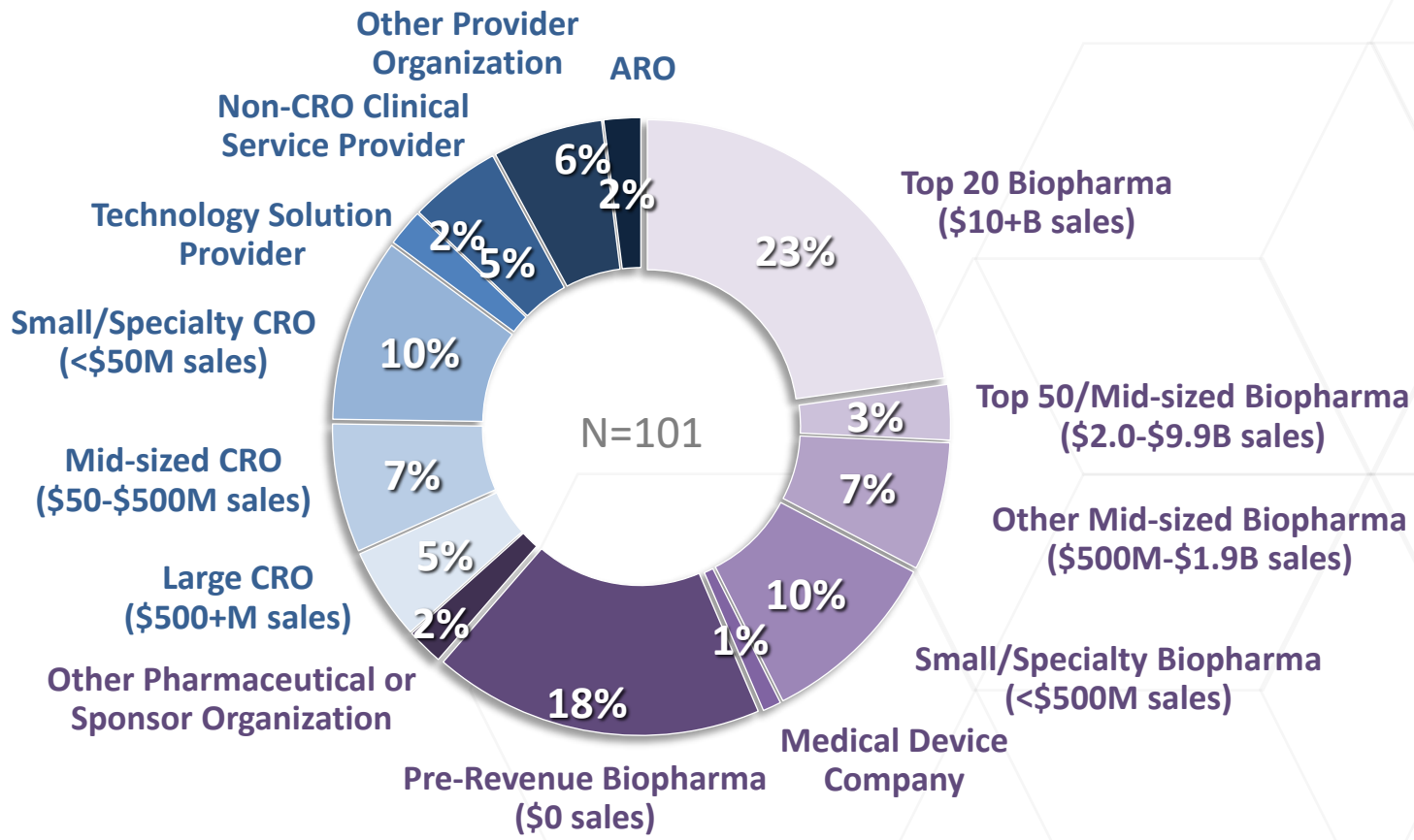
AbbVie	Cyclerion Therapeutics, Inc.	Istari Oncology	PopsiCube
Acrivon Therapeutics	Cyteir	Janssen	Premier Research
Agenus	Daiichi Sankyo	Javara Inc.	REGENXBIO
Akebia	Denver Arthritis Clinic	Julius Clinical	Richmond Pharmacology
Angion Biomedica	DP Clinical	Kiniksa Pharmaceuticals	Sanofi
Arcus Bioscience	Emalex Biosciences	Kura Oncology	Sarah Cannon Research Institute
Astellas	EMD Serono	LabCorp Drug Development	Sofpromed
AstraZeneca	Epizyme	Lynn Institute of Denver	SubjectWell
Atox Bio	Excelsior Medical Group	Mangan Consulting, Inc.	Sumitomo Dainippon Pharma
Aurobindo Pharma Ltd.	F2G	Medable	Swiss TPH
Baxter Healthcare	Ferring	Merck	Syneos Health
Bayer	FHI 360	Mitsubishi Tanabe	TYRA Biosciences
Beam Therapeutics	G1 Therapeutics	Neurological Associates of Albany	University of Rochester, Wilmot Cancer Inst.
Benchmark Research	George Clinical Pty Ltd	Novartis	University of Utah
BMS	GSK	Novo Nordisk	VBL Therapeutics
Boehringer Ingelheim	HUTCHMED International Corp.	ONO Pharmaceutical Co.Ltd.	Virgin Media
Cerevel Therapeutics, LLC	IAVI	Orion Corporation	Virginia Commonwealth University
Clinical QA Intl LLC	ICON	Orion Pharma	WCG Clinical
Clinipace	ICON Central Laboratories	Palvella	X4 Pharmaceuticals
CuraSen Therapeutics, Inc.	inSeption Group, LLC	Pfizer	Zymeworks

Respondent Characteristics

- There were 101 respondents, 64 representing sponsor companies, 35 representing provider companies, and 2 representing Academic Research Organizations.
- Thirty-six percent (36%) of the survey respondents representing sponsors worked for companies in the Top 20 biopharmas in terms of revenue. Respondents representing providers worked for a wide range of provider types, most commonly CROs (63%).
- Thirty-eight percent (38%) of the respondents represented Clinical Development/Operations; slightly more than a third represented Quality Assurance (34%); and the remainder represented a wide spectrum of management and functional roles.
- Respondents represented companies that sponsored or conducted a variable number of clinical trials in 2021, from more than 50 (37%) to 1 to 5 (19%) trials. A very small number of respondents represented companies that conducted or sponsored no clinical trials at all that year.
- The vast majority of respondents resided in the US and worked for companies that were headquartered there, most commonly in the Northeast and Southeast. Approximately one-fifth had headquarters in Northern Europe or Japan.
- Where numbers allowed, subset analyses were performed by all of the above variables to examine trends by respondent and company type. Only selected highlights of these analyses are provided in this report.

Respondent Characteristics

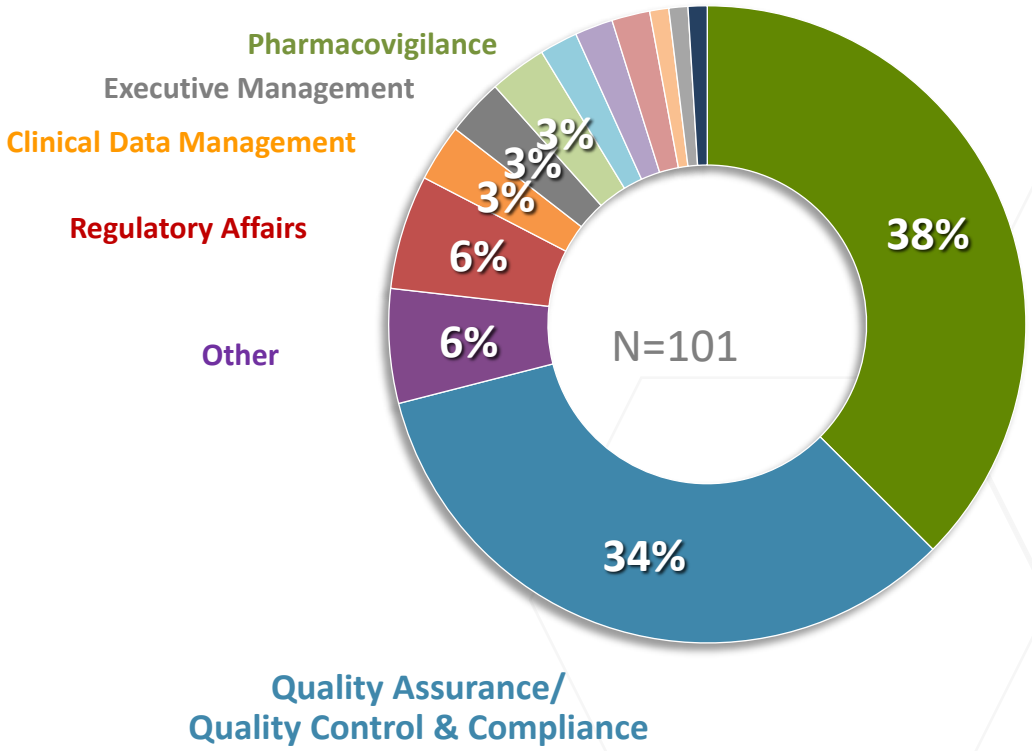
Company Type



Q: Please indicate your company type.

Respondent Characteristics

Functional Area

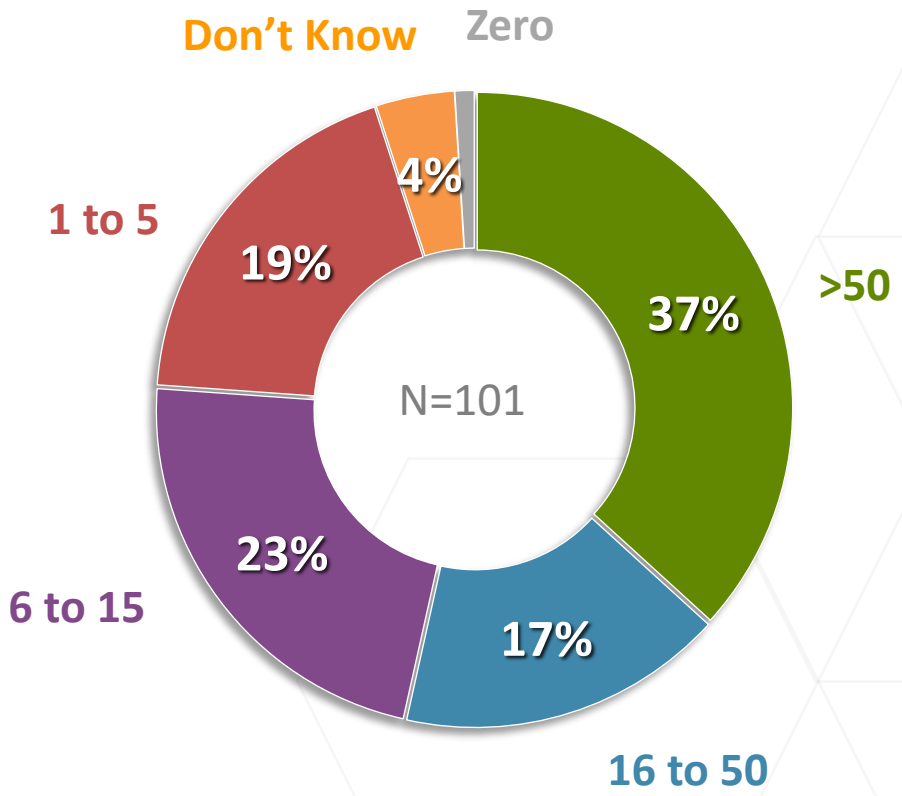


2%	1%
Medical Affairs/Scientific	Alliance Management/ Partnering
Patient Advocacy/Patient Engagement	Biostatistics/ Statistical Programming
Procurement/ Outsourcing/ Vendor Management	Business Development

Q: What is the functional area in which you work?

Respondent Characteristics

Number of Clinical Trials Sponsored or Supported in 2021

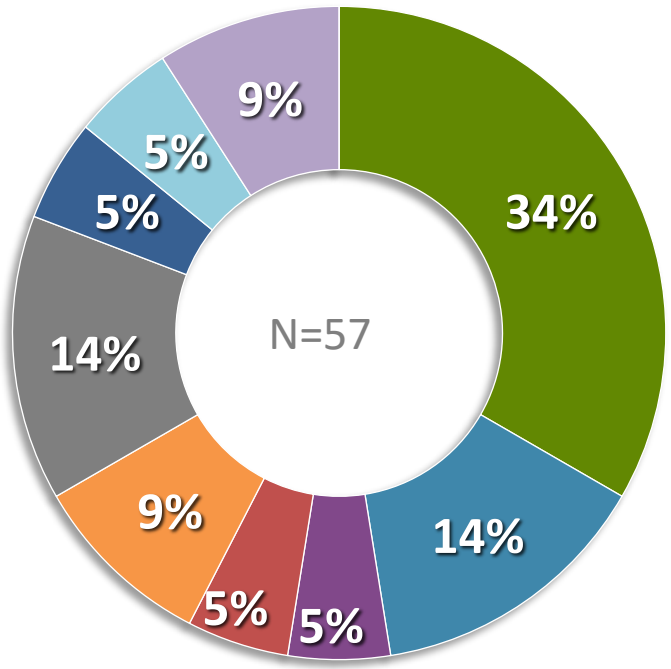


Q: In 2021, approximately how many clinical trials will your company sponsor, or support through services you offer?

Respondent Characteristics

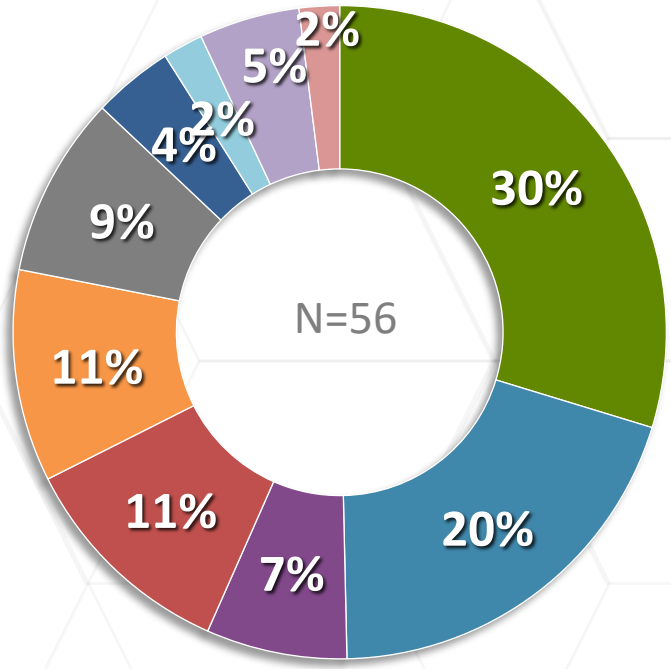
Geographic Area

Company Headquartered



US Northeast
US Southeast
US Southwest
US Midwest
US West
Northern Europe
Southern Europe
Japan
Other
Eastern Europe

Specifically Located



Q: In which geographic area: ...is your company headquartered? ...are you specifically located?

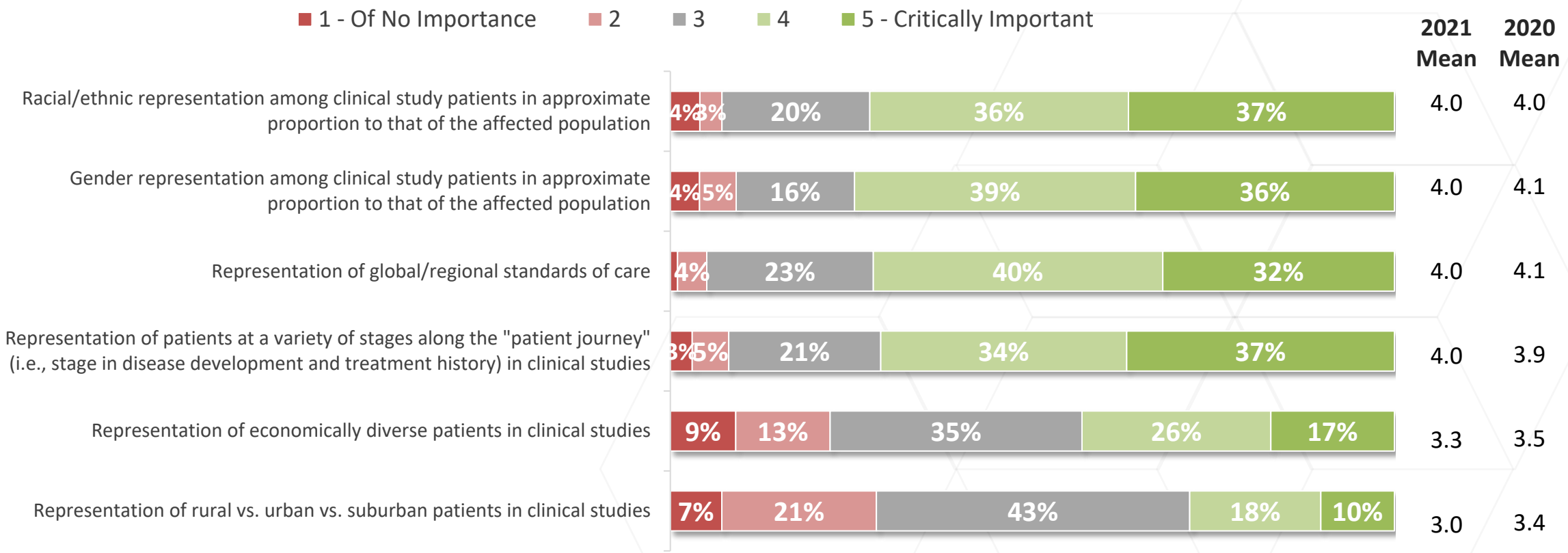
Diversity in Clinical Trial Participation

Diversity in Clinical Trial Participation

- As in the 2020 Avoca Industry Survey, respondents in 2021 were asked how critical to the quality of clinical research they considered each of several different types of diversity among trial participants. On average, respondents in 2021 felt approximately equally strongly about diversity with respect to each of race/ethnicity, gender, global/regional standards of care, and disease stage; these were thought by most to be at least somewhat important and by ~ one-third to be critical to quality. Respondents were more divided when it came to economic diversity and population type (rural/urban/suburban). Except in the cases of race and disease stage, respondents on average felt *less* strongly about diversity in 2021 than they had in 2020.
- When asked how each of their own companies and the industry as a whole were performing in each area of clinical trial subject diversity, respondents on average perceived their own companies to have middling levels of performance and the rest of the industry to be performing more poorly. Performance with respect to gender diversity and global/regional standards of care was felt in 2021 to have been about the same as in 2020, and performance regarding diversity in disease stage was felt to have improved. However, performance with respect to racial diversity, economic diversity, and diversity in population type (rural/suburban/urban) was on average rated more poorly in 2021 than it had been in 2020.
- Given the generally mediocre performance in this area as judged by respondents, it is not surprising that fewer respondents were familiar with the FDA Guidance on Enhancing the Diversity of Clinical Trial Populations (53%) than with other FDA or ICH Guidance documents relevant to their work. Although this fraction was higher in 2021 than it had been in 2020, this was also true for every other Guidance document studied.

Diversity in Clinical Trial Participation: Importance

Please rate how critical to the quality of clinical research you consider each of the following, using a scale from 1 (of no importance) to 5 (critically important)



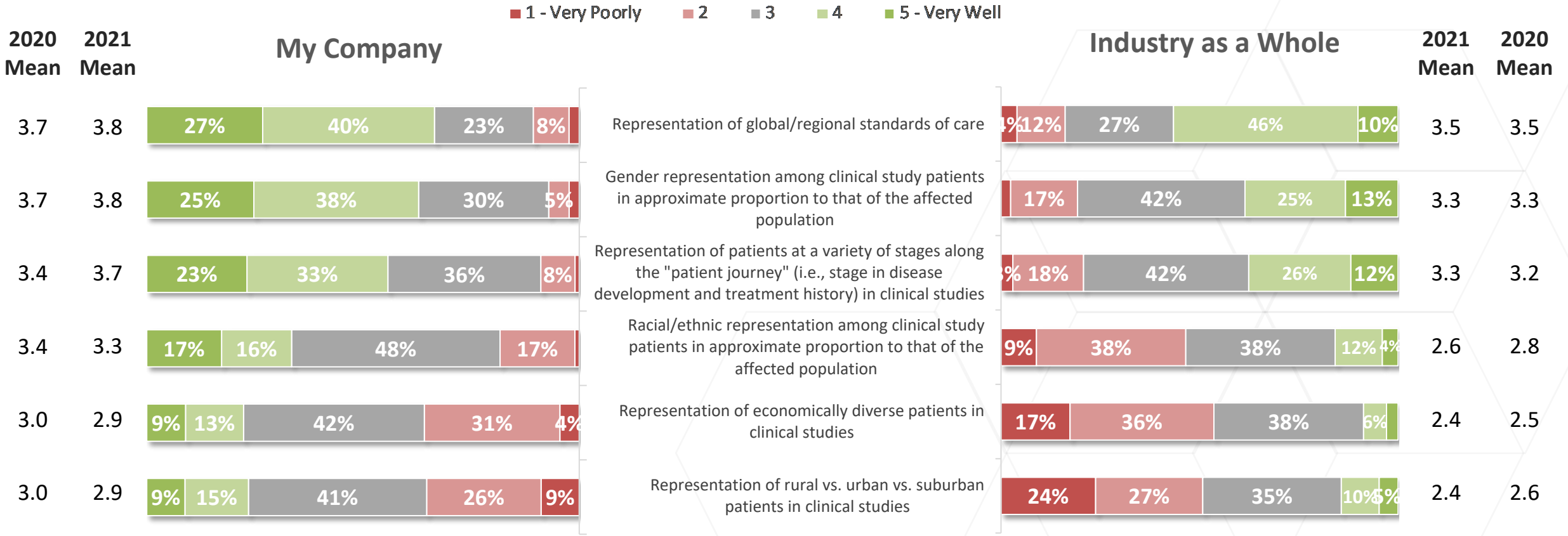
N 2021: 98; N 2020: 211-215
Q: Please rate how critical to the quality of clinical research you consider each of the following, using a scale from 1 (of no importance) to 5 (critically important)

Diversity in Clinical Trial Participation: Verbatim

- Seventeen (17) respondents provided open-ended comments to supplement their ratings to this question.
- While most agreed that a diverse group of study participants was desirable, some did not have the resources to prioritize increased diversity, and some trials were too specific to necessitate more diversity.
- Several mentioned the importance of ethics, while others emphasized that following the science is key and that study participant diversity is paramount when drug candidates are important in all populations.
    - "If there is a scientific reason that a socioeconomic or population density concern may represent a change in efficacy and safety, then it … does make sense to recruit and stratify accordingly."
    - One would, however, "need to determine statistically how many subjects of the various races or economic groups are needed to answer questions and then select sites that can deliver," because "mixing races into studies according to existing percentages is not the scientific way to determine if the disease and patients respond to a drug in a different manner."

Diversity in Clinical Trial Participation: Performance

Overall, what are your perceptions of how your company, and the drug development industry as a whole, are performing in each of the following areas?



N 2021: 63-85; N 2020: 208-213

Q: Overall, what are your perceptions of how each of your company, and the drug development industry as a whole, are performing in each of the following areas, using a scale from 1 (very poorly) to 5 (very well)?

Diversity in Clinical Trial Participation: Performance by Company Type

Mean Rating

	Top 20 Biopharma ($10+ billion sales)	Top 50/ Mid-sized Biopharma ($2.0 - $9.9 billion sales)	Other Mid-sized Biopharma ($500 million - $1.9 billion sales)	Small/ Specialty Biopharma (<$500 million sales)	Pre-Revenue Biopharma ($0 sales)	Large CRO	Mid-sized CRO ($50 - $500 million sales)	Small/ Specialty CRO (<$50 million sales)	Non-CRO Clinical Service Provider	Other Provider Organization
N	**23**	**3**	**7**	**10**	**18**	**5**	**7**	**10**	**5**	**6**
Racial/ethnic representation among clinical study patients in approximate proportion to that of the affected population	3.4	4.7	3.6	2.8	3.2	2.8	2.8	3.3	4.3	3.6
Gender representation among clinical study patients in approximate proportion to that of the affected population	3.9	4.0	4.1	3.5	4.0	3.0	3.6	3.1	4.7	4.2
Representation of economically diverse patients in clinical studies	3.0	3.3	3.3	3.0	3.0	2.7	2.5	2.4	3.3	3.2
Representation of rural vs. urban vs. suburban patients in clinical studies	2.8	3.0	3.6	2.5	2.9	2.3	2.3	2.4	4.7	3.8
Representation of patients at a variety of stages along the "patient journey" (i.e., stage in disease development and treatment history)	3.8	3.0	4.0	3.6	3.8	3.7	3.5	3.7	3.0	4.0
Representation of global/regional standards of care	3.9	4.7	3.8	3.4	3.8	3.7	3.5	3.4	5.0	4.0

Q: Overall, what are your perceptions of how each of your company, and the drug development industry as a whole, are performing in each of the following areas, using a scale from 1 (very poorly) to 5 (very well)? **Green=Mean rating in positive range, >3.3 units**

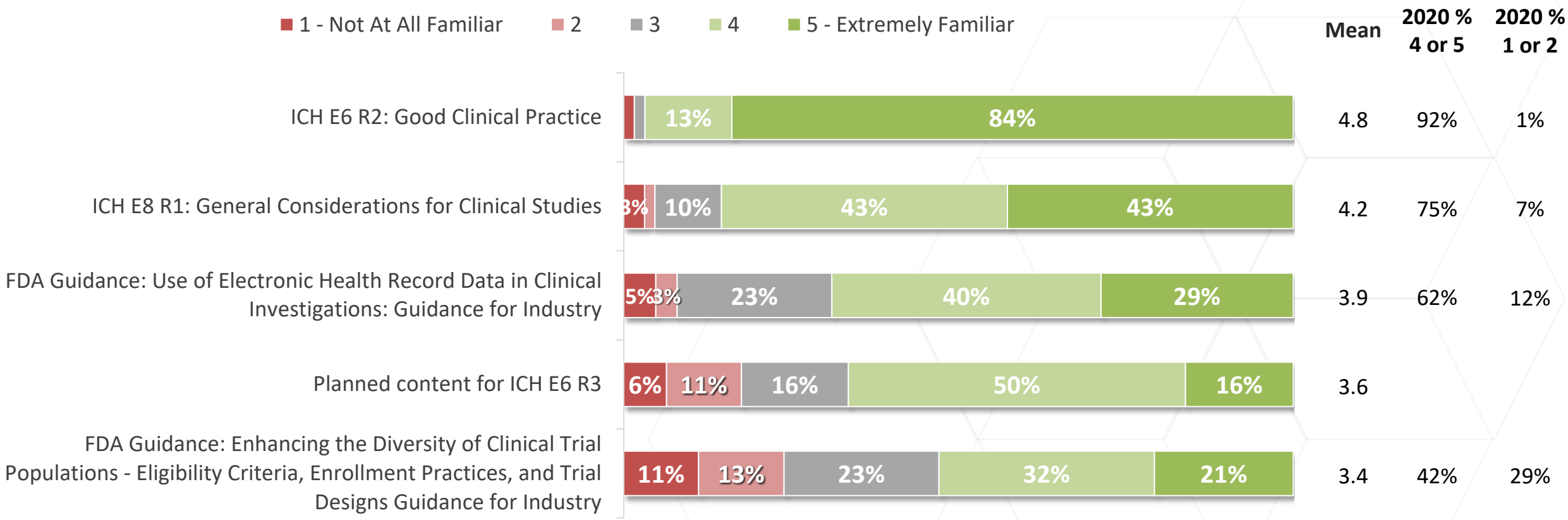
Diversity in Clinical Trial Participation: Performance by Trial Volume

	Mean Rating				
	>50	16 to 50	6 to 15	1 to 5	Zero
N	**37**	**17**	**23**	**19**	**1**
Racial/ethnic representation among clinical study patients in approximate proportion to that of the affected population	3.3	3.4	3.3	3.1	3.0
Gender representation among clinical study patients in approximate proportion to that of the affected population	3.8	3.5	3.8	4.1	3.0
Representation of economically diverse patients in clinical studies	3.0	2.8	2.8	2.9	3.0
Representation of rural vs. urban vs. suburban patients in clinical studies	2.9	2.6	2.7	3.3	3.0
Representation of patients at a variety of stages along the "patient journey" (i.e., stage in disease development and treatment history)	3.8	3.7	3.9	3.3	3.0
Representation of global/regional standards of care	3.9	3.8	3.7	3.7	5.0

Q: Overall, what are your perceptions of how each of your company, and the drug development industry as a whole, are performing in each of the following areas, using a scale from 1 (very poorly) to 5 (very well)? **Green=Mean rating in positive range, >3.3 units**

Diversity in Clinical Trial Participation: Relative Knowledge

Familiarity with Guidance Documents



N: 62-63
Q: How would you rate your familiarity with each of the following Guidance documents?

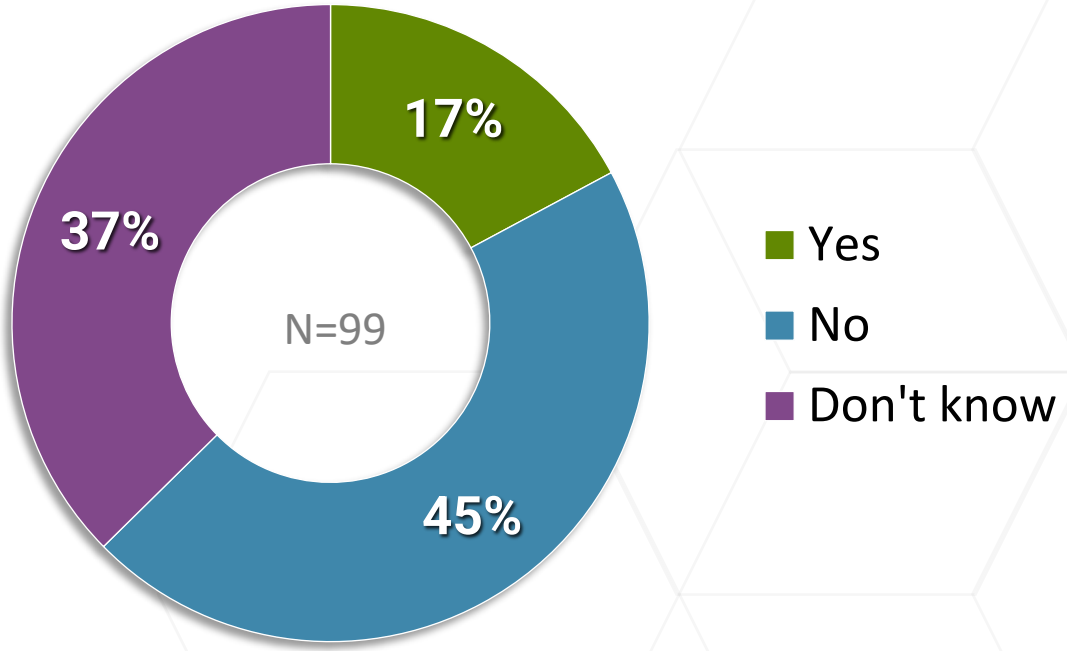
Perspectives on Regulators and Clinical Trial Participant Diversity

Perspectives on Regulators and Clinical Trial Participant Diversity

- Only a minority (17%) of respondents were aware of their companies having had interactions with regulators over the last two years specifically on the topic of clinical trial participant diversity.
- Nevertheless, most respondents had opinions about how the emphasis placed by regulatory authorities on clinical trial participant diversity might evolve over the coming 5 years.
  - Across all three regulatory bodies about which they were questioned (US FDA, EU EMA, Japan PMDA), there was on average a “best guess” among respondents that regulatory bodies would place increasing emphasis on diversity in clinical trial participants.
  - However, for some regulatory authorities and some aspects of participant diversity, opinions among respondents were quite divided. This was especially the case across regulatory authorities for diversity with respect to population type (rural/urban/suburban), and for many aspects of diversity within Japan’s PMDA.

Diversity Among Trial Participants: Interactions with Regulators

Over the last two years, has your company had interactions with regulators specifically on the topic of participant diversity in its clinical studies?



Q: Over the last two years, has your company had interactions with regulators specifically on the topic of participant diversity in its clinical studies?

Diversity Among Trial Participants: Perceived Regulatory Perspectives

"Best guesses" as to How the Requirements of Regulatory Bodies will Change over the Next 5 Years with Respect to Each Aspect of Diversity in Clinical Research Participation.

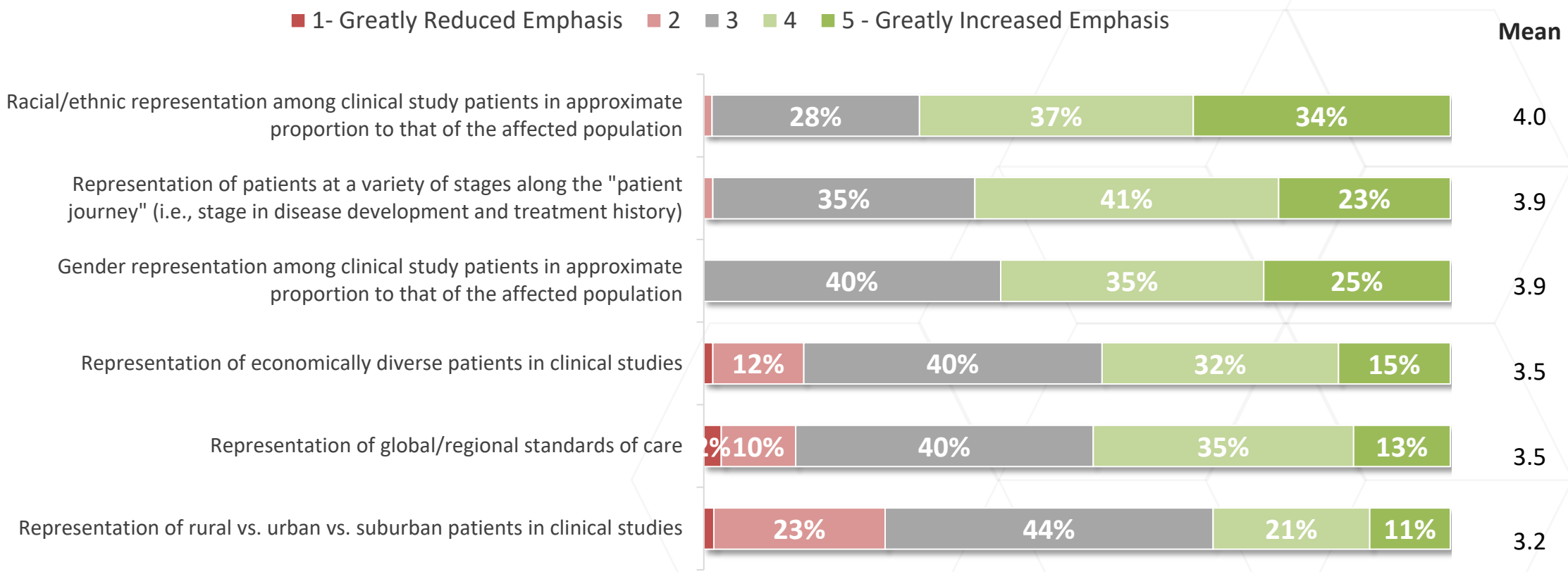
Mean ratings on a scale of 1 (greatly reduced emphasis) to 5 (greatly increased emphasis)

	US FDA	EU EMA	Japan PMDA
N	**75-89**	**66-83**	**51-62**
Gender representation among clinical study patients in approximate proportion to that of the affected population	3.9	3.8	3.2
Racial/ethnic representation among clinical study patients in approximate proportion to that of the affected population	4.0	3.8	3.0
Representation of economically diverse patients in clinical studies	3.5	3.4	3.0
Representation of global/regional standards of care	3.5	3.7	3.3
Representation of patients at a variety of stages along the "patient journey" (i.e., stage in disease development and treatment history)	3.9	3.7	3.5
Representation of rural vs. urban vs. suburban patients in clinical studies	3.2	3.1	2.9

Diversity Among Trial Participants: Perceived Regulatory Perspectives

"Best Guesses" regarding Changes in Regulatory Requirements Over 5 Years

US FDA

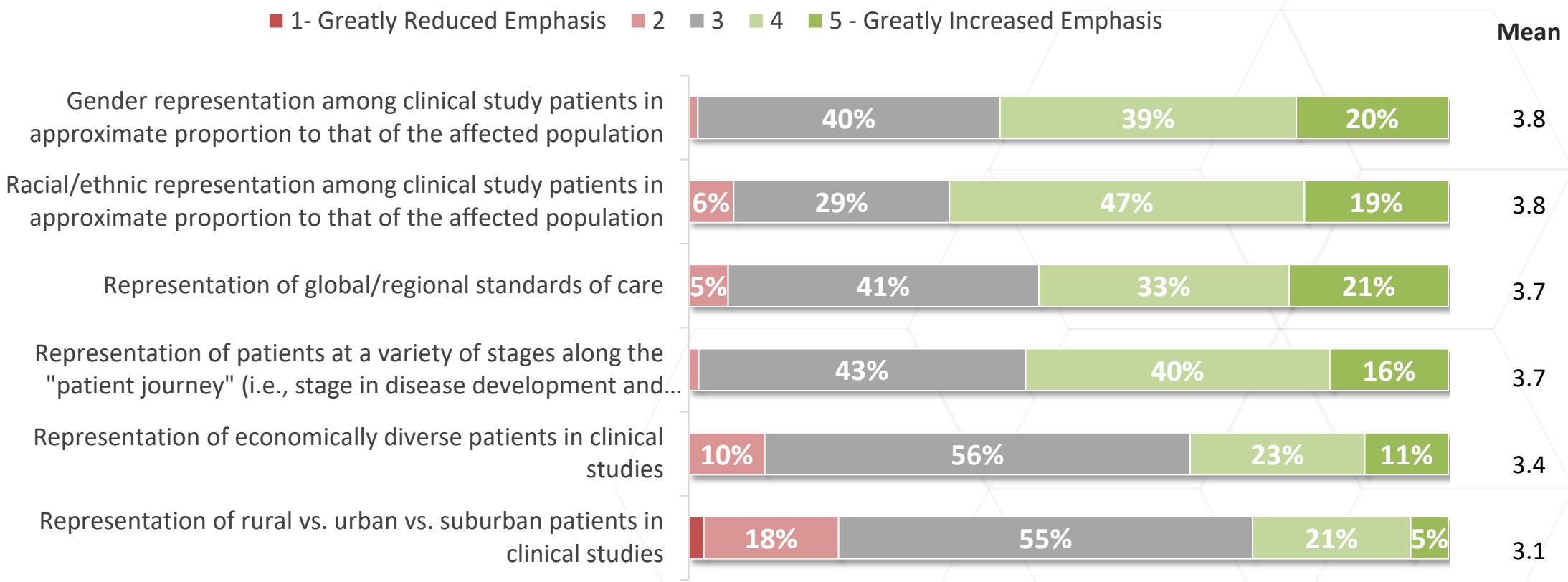


N: 73-89

Q: Please provide your "best guess" as to how the requirements of each regulatory body will change over the next 5 years with respect to each of the following aspects of diversity in clinical research participation, on a scale of 1 (greatly reduced emphasis) to 5 (greatly increased emphasis)

Diversity Among Trial Participants: Perceived Regulatory Perspectives

"Best Guesses" regarding Changes in Regulatory Requirements Over 5 Years
EU EMA

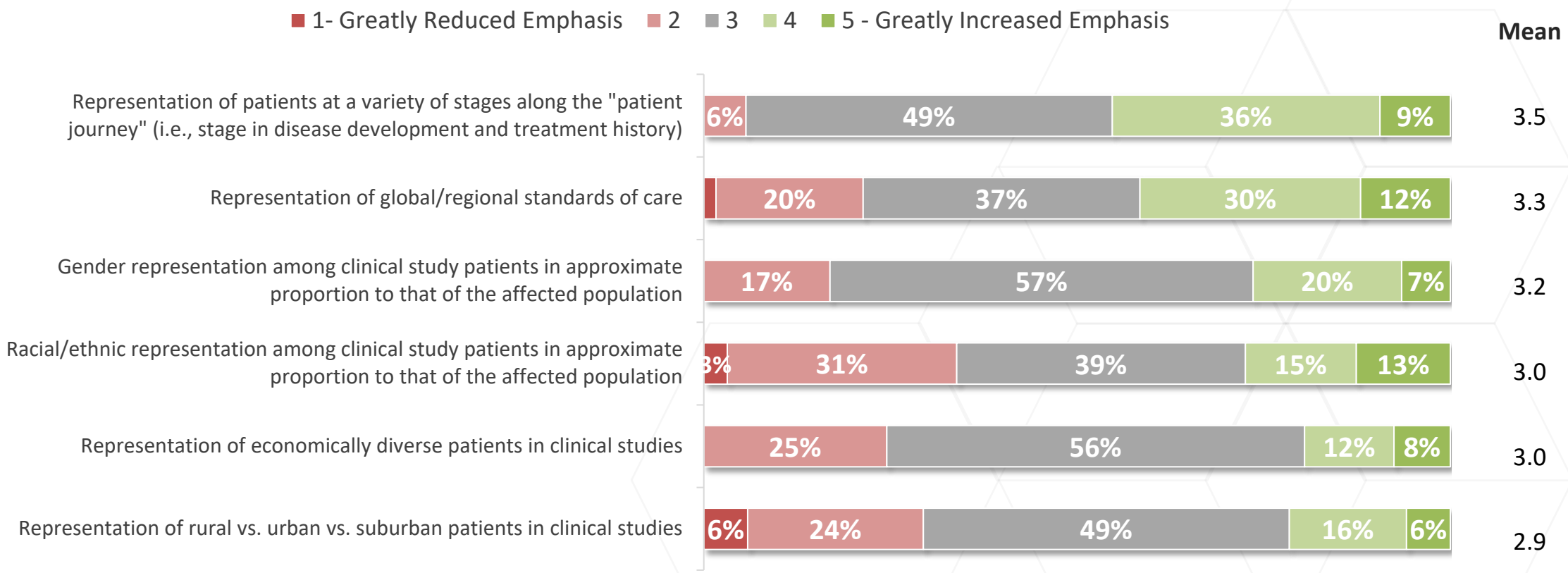


N: 66-83

Q: Please provide your "best guess" as to how the requirements of each regulatory body will change over the next 5 years with respect to each of the following aspects of diversity in clinical research participation, on a scale of 1 (greatly reduced emphasis) to 5 (greatly increased emphasis)

Diversity Among Trial Participants: Perceived Regulatory Perspectives

"Best Guesses" regarding Changes in Regulatory Requirements Over 5 Years
Japan PMDA



N: 51-62
Q: Please provide your "best guess" as to how the requirements of each regulatory body will change over the next 5 years with respect to each of the following aspects of diversity in clinical research participation, on a scale of 1 (greatly reduced emphasis) to 5 (greatly increased emphasis)

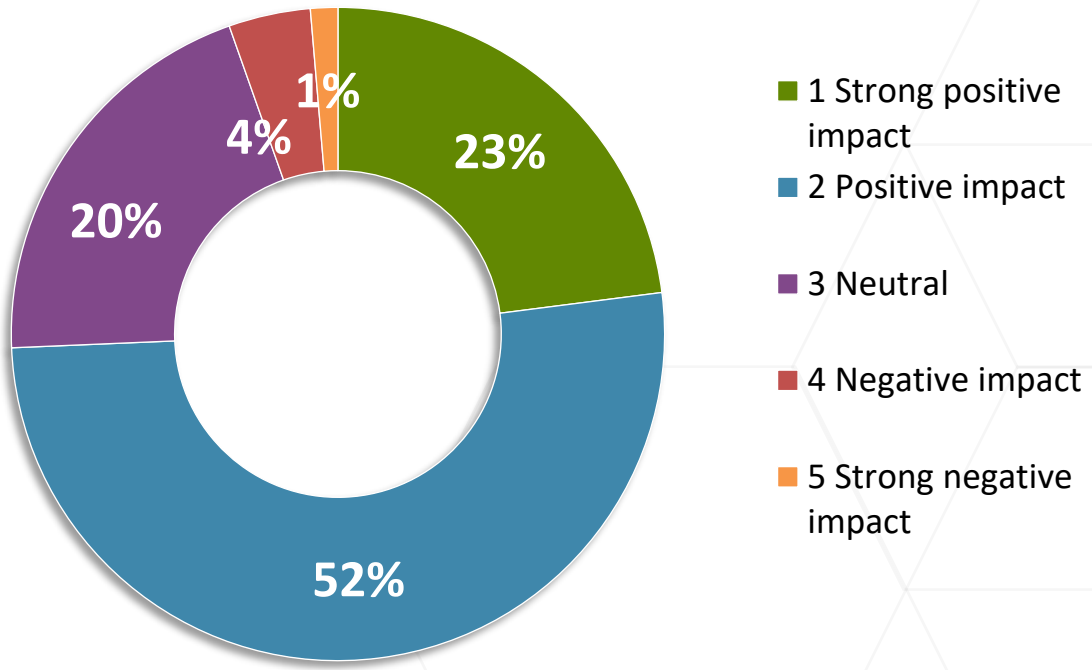
Impact of Variability and Flexibility in Clinical Trial Execution on Clinical Trial Participant Diversity

Impact of Variability and Flexibility in Clinical Trial Execution on Clinical Trial Participant Diversity

- Even in the absence of quotas dictated by regulatory bodies, respondents overwhelmingly expected that participant diversity in clinical studies could and would be positively impacted by variability and flexibility in how clinical research is executed. Only 5% of respondents felt that this force might have a negative impact on participant diversity.
- For many respondents, however, this perception was aspirational; in no area of clinical trial execution did more than a slight majority report that their companies had reached the optimum level of executional flexibility to support participant diversity, and in most executional areas this was a minority. Only about 1 in 6 respondents perceived their organizations to have greater than optimal levels of variability/flexibility in any area; most who were not at the optimum reported too little rather than too much.
- With respect to specific operational approaches, respondents were most likely to report that their organizations were at the optimal level of variability/flexibility to support participant diversity when it came to study staff-patient interactions, followed by overall operationalization tactics *within* an individual clinical trial (i.e., hybrid approaches to decentralization, patient engagement, etc.). Variability and flexibility were most likely to be suboptimal in the areas of laboratory sample collection and overall operationalization of clinical trials *across* a development program (i.e., use of decentralized approaches for some trials).
- Among company types, provider organizations and Top 20 or pre-revenue biopharma – those with very high or low trial volumes - were generally most likely to be near optimal levels of variability and flexibility.

Variability and Flexibility in Clinical Trial Execution vs. Participant Diversity

In the absence of "quotas" dictated by regulatory bodies, to what extent do you believe that participant diversity in clinical studies is or will be positively impacted by variability and flexibility in how clinical research is executed?



N: 74

Q: In the absence of "quotas" dictated by regulatory bodies, to what extent do you believe that participant diversity in clinical studies is or will be positively impacted by variability and flexibility in how clinical research is executed?

Impact of Variability and Flexibility in Clinical Trial Execution on Clinical Trial Participant Diversity: Verbatim

What do you see as the key challenges associated with variability and flexibility in clinical trial execution?

- Forty-nine respondents answered this question.
  - In general, their perception was that the industry is conservative and inflexible, fearing change, being rigid and “stuck in the old ways of working” with “upper management stagnation.”
    - "It seems that it is easier to go with what you know rather than learning something new.”
  - This challenge is accompanied by a strong desire to maintain consistency in scientific standards and reliability/quality of data.
  - Other concerns included:
    - Regulatory restrictions
    - Funding vis-á-vis costs associated with including more sites to achieve diversity
    - Earning trust in diverse communities
    - Recruitment and training (including in technology)—staff are extremely busy
    - Complex protocols

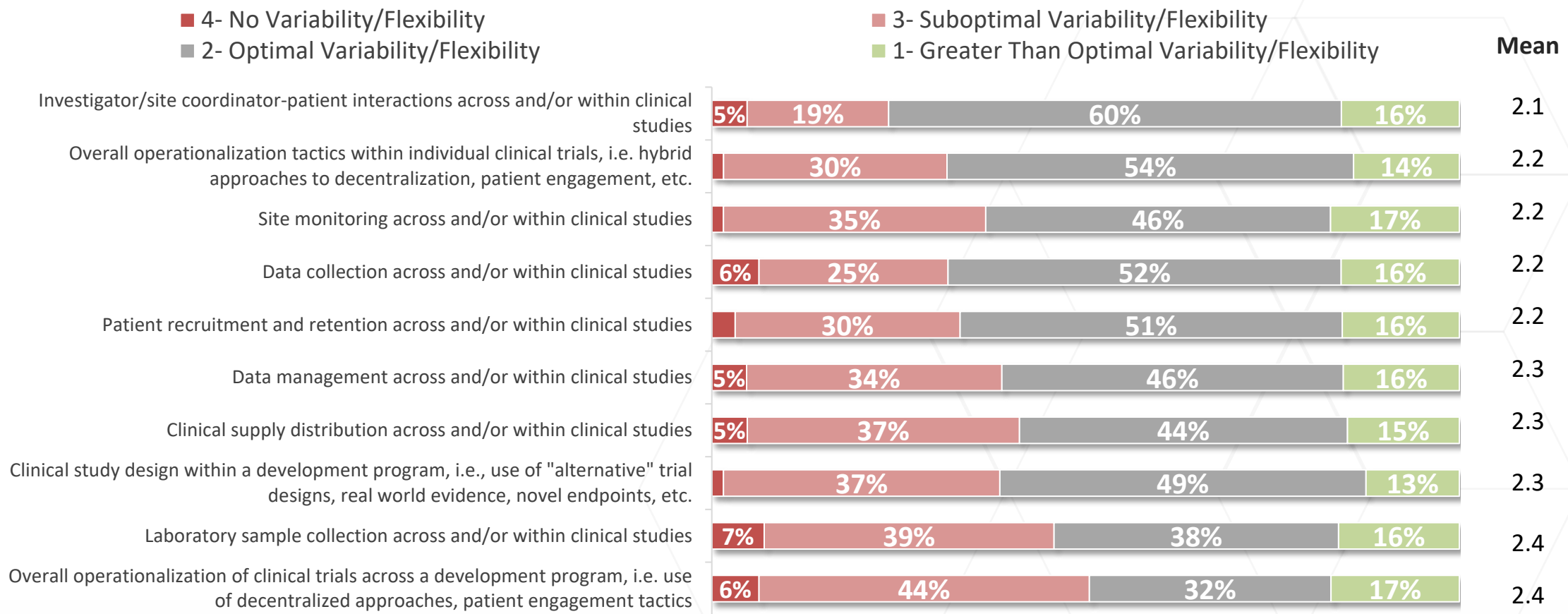
Impact of Variability and Flexibility in Clinical Trial Execution on Clinical Trial Participant Diversity: Verbatim

What do you see as the key enablers of variability and flexibility in clinical trial execution?

- Forty-seven respondents answered this question.
  - Many believed that good regulations, and imaginative use of technology and other tools, were helpful. Old, burdensome regulations should be dropped.
  - Other important enablers included:
    - Understanding risk levels, and willingness to take some risks, as with the pandemic experience
    - Sponsor, management, PI, and team flexibility
    - Vendor reliability
    - Data availability
    - Good patient relationships that retain trial participants
    - Sharing of successes and lessons learned, perhaps from novel trial designs
    - Creative personnel with critical thinking skills; increased staffing to lighten the load
    - Regulatory flexibility and guidance

Variability/Flexibility in Clinical Trial Execution – Nearness to Optimum

Compared to your perception of the optimal level of executional variability and flexibility, how would you rate your company's clinical development programs in terms of variability and flexibility in approaches to...



N=61-63

Q: Compared to your perception of the optimal level of executional variability and flexibility, how would you rate your company's clinical development programs in terms of variability and flexibility in approaches to...:

Variability/Flexibility in Clinical Trial Execution – Nearness to Optimum by Company Type

Mean Rating

	Top 20 Biopharma ($10+ billion sales)	Top 50/ Mid-sized Biopharma ($2.0 - $9.9 billion sales)	Other Mid-sized Biopharma ($500 million - $1.9 billion sales)	Small/ Specialty Biopharma (<$500 million sales)	Pre-Revenue Biopharma ($0 sales)	Large CRO	Mid-sized CRO ($50 - $500 million sales)	Small/ Specialty CRO (<$50 million sales)	Non-CRO Clinical Service Provider	Other Provider Organization
N	**23**	**3**	**7**	**10**	**18**	**5**	**7**	**10**	**5**	**6**
Clinical study design within a development program, i.e., use of "alternative" trial designs, real world evidence, novel endpoints, etc.	2.3	2.5	2.6	2.9	2.1	2.5	2.0	2.1	1.8	2.3
Overall operationalization of clinical trials across a development program, i.e., use of decentralized approaches, patient engagement tactics	2.5	2.5	2.8	2.8	2.1	2.5	2.5	2.3	2.0	2.5
Overall operationalization tactics within individual clinical trials, i.e., hybrid approaches to decentralization, patient engagement, etc.	2.3	2.5	2.8	2.5	1.9	1.7	3.0	2.0	1.8	2.0
Data collection across and/or within clinical studies	2.3	2.5	2.6	2.6	2.1	2.0	2.0	1.9	1.5	2.5
Data management across and/or within clinical studies	2.4	2.5	2.8	2.6	2.3	2.0	2.0	1.6	1.5	2.5
Site monitoring across and/or within clinical studies	2.0	2.5	2.8	2.8	2.2	1.7	2.0	2.0	1.8	2.0
Clinical supply distribution across and/or within clinical studies	2.0	2.5	2.8	2.8	2.2	2.0	2.0	2.1	2.0	2.3
Laboratory sample collection across and/or within clinical studies	2.1	2.5	2.8	2.8	2.2	1.5	2.0	2.4	2.3	2.7
Investigator/site coordinator-patient interactions across and/or within clinical studies	2.0	2.5	2.6	2.5	2.0	2.0	2.0	1.9	1.5	2.3
Patient recruitment and retention across and/or within clinical studies	2.3	2.0	2.6	2.6	2.4	2.3	2.0	1.7	1.5	1.8

Q: Compared to your perception of the optimal level of executional variability and flexibility, how would you rate your company's clinical development programs in terms of variability and flexibility in approaches to… **Yellow= Not Flexible Enough (>0.2 units from the optimum), Green= Optimal Flexibility, Blue= Too Flexible (>0.2 units from the optimum)**

Variability/Flexibility in Clinical Trial Execution – Nearness to Optimum by Trial Volume

Mean Rating

	>50	16 to 50	6 to 15	1 to 5
N	**37**	**17**	**23**	**19**
Clinical study design within a development program, i.e., use of "alternative" trial designs, real world evidence, novel endpoints, etc.	2.1	2.5	2.4	2.0
Overall operationalization of clinical trials across a development program, i.e., use of decentralized approaches, patient engagement tactics	2.3	2.8	2.4	2.0
Overall operationalization tactics within individual clinical trials, i.e., hybrid approaches to decentralization, patient engagement, etc.	2.1	2.5	2.1	2.0
Data collection across and/or within clinical studies	2.2	2.3	2.2	2.0
Data management across and/or within clinical studies	2.2	2.4	2.4	2.1
Site monitoring across and/or within clinical studies	1.9	2.3	2.4	2.1
Clinical supply distribution across and/or within clinical studies	2.2	2.1	2.6	2.2
Laboratory sample collection across and/or within clinical studies	1.9	2.5	2.6	2.2
Investigator/site coordinator-patient interactions across and/or within clinical studies	1.9	2.2	2.2	1.8
Patient recruitment and retention across and/or within clinical studies	2.2	2.1	2.3	2.2

Q: Compared to your perception of the optimal level of executional variability and flexibility, how would you rate your company's clinical development programs in terms of variability and flexibility in approaches to… **Yellow= Not Flexible Enough (>0.2 units from the optimum), Green= Optimal Flexibility**

In your experience, what are the best ways to promote diversity in clinical research participation with respect to *racial/ethnic representation*?

- The most common advice from the 45 respondents to this question was to select geographic sites that have a diverse demographic and to gain trust from that community: “Come to them vs. them coming to you.”
- This can be achieved by increasing representation of racially and ethnically diverse researchers and doctors, and by engaging community leaders and advocacy groups--“Strong community engagement programs at the site level that include key gatekeepers for the particular participant population.”
- Other suggestions included:
  - Provide resources, compensation, childcare that enable retention
  - Use targeted advertising, including social media platforms
  - Communicate information adequately and appropriately

In your experience, what are the best ways to promote diversity in clinical research participation with respect to *gender representation*?

- Among the 42 respondents to this question, a common answer was to increase gender representation within the institutions.
- However, the nature of the disease and study design may sometimes preclude gender diversity: “One should not automatically assume equal gender representation.”
- In addition, reproductive concerns affect females disproportionately - female patients may need to stop participation if they become pregnant, or be more concerned about or susceptible to reproductive health risks.
- Researchers should also recognize the time-constraint challenges of many women: “Recruitment needs to emulate customer acquisition strategies from other industries. When we treat patients like customers—articulating the study’s value, holding the patient’s hands throughout the entire enrollment process, and letting patients choose their method of care from a large selection of trials—we get more diversity.”
- Other recommendations:
  - Engage with patient advocacy groups
  - Target recruiting and advertising, including social media platforms, and identify the benefit of participation
  - Criteria need to be amended to include transgender and intersex populations

In your experience, what are the best ways to promote diversity in clinical research participation with respect to *representation of economically diverse patients*?

- Among the 46 respondents, the most common responses involved site selection with respect to location, accessibility, and patients' comfort level in going to the sites.
- Participation should be facilitated with scheduled transportation, gas cards, and/or off-hours or home visits. In addition:
  - Community medical centers should be considered
  - Use of diverse clinical staff to create a comfortable environment at the sites
  - Get NGOs (non-governmental organizations, e.g. patient advocacy) into discussion before trial design
  - Ensure that healthcare is the same across the groups
  - Involve advocacy groups and other local leaders for support and communication, if necessary
  - Include larger healthcare systems
  - Emulate customer acquisition strategies used by other industries
  - Use appropriate brochures and other sources of information
  - Establish trust in pharma companies and their work
- Two caveats:
  - If sponsors are not willing to bear the cost for participation of uninsured individuals in clinical trials, economic diversity will not be reached.
  - Patients without regular access to medical care might not have the necessary medical history the studies require.

In your experience, what are the best ways to promote diversity in clinical research participation with respect to *representation of rural vs. urban vs. suburban patients*?

- The 42 respondents again most often mentioned site selection/location to support recruitment of the rural population.
- Transportation for patients was often mentioned - supporting travel to study sites
- Other mentions:
  - Sponsor willingness to accommodate funding for rural sites
  - Conduct outreach in appropriate places by people who can relate to the community
  - Consider telemedicine due to loss of rural clinics

In your experience, what are the best ways to promote diversity in clinical research participation with respect to *representation of patients at a variety of stages along the "patient journey"*?

- The 40 respondents to this question did not provide a unified voice.
  - Three mentioned the need for effective inclusion/exclusion (I/E) criteria, including that the different disease stages should be considered.
  - Another favored better explaining the benefits of clinical trials and communicating clinical trial availabilities to physicians and insurance companies.
  - Other suggestions:
    - Tap into patient advocacy and support groups at the protocol development stage
    - Consult regulatory guidelines
    - Incorporate patients' insights at the start of a trial and integrate into study designs
    - Record patient stories/progress via video

In your experience, what are the best ways to promote diversity in clinical research participation with respect to *representation of global/regional standards of care*?

- The 35 respondents again varied in their responses.
- Some mentioned that unequal healthcare standards around the globe make this a tough issue. “After a drug is approved, there needs to be an incentive to study the drug in a population with a different standard of care.” Companies should ensure that investigators comply with protocols and that protocols align with standards of care.
- Some suggested use of a core protocol with regional variations – though some did not condone this idea.
- Also:
  - Increase knowledge about respective global/regional standards of care through education
  - Ensure that proposed marketing strategy takes global payers and patients into account

Decentralized Clinical Trial Activities and Participant Diversity

Decentralized Clinical Trial Activities and Participant Diversity

- On average, every executional tactic relating to *clinical trial decentralization* was perceived by respondents to have a positive impact on clinical trial participant diversity with respect to every demographic and disease-related variable.
- The tactics felt to have the most positive impacts were those that brought study-related medical care to convenient locations for participants: home healthcare provider study visits, point-of-care integration of clinical research (i.e., performance of trial procedures at usual points of care), study visits by telemedicine, and ship-to-home of clinical supplies. These were felt to be particularly impactful when it came to racial, economic, and population type (urban vs. rural) diversity.
- Online or wearable trial features (e-consent; wearables; patient portals, communities, or diaries; and completely site-less trials) were on average thought to be slightly less, but still positively, impactful.

Decentralized Clinical Trial Activities and Participant Diversity

On a scale from 1 (substantial risk to participant diversity) to 5 (substantial benefit to participant diversity), how do you perceive each of the below (executional tactics) to impact diversity in clinical research participation (with respect to each of the following demographic/disease variables)?

Mean Rating

Tactic \\ Demographic or Disease Variable	Race	Gender	Socio-economic	Rural vs. urban vs. suburban	Stage of patient journey	Global/ regional standards of care
Home healthcare provider study visits	4.3	4.0	4.2	4.3	4.1	3.8
Point-of-care integration of clinical research, i.e., performance of trial procedures at usual points of care	4.2	4.1	4.2	4.2	4.2	3.9
Ship-to-home of clinical supplies	4.1	4.0	4.0	4.2	3.9	3.7
Study visits by telemedicine	4.0	3.9	3.9	4.2	3.9	3.8
Hybrid trials (mix of decentralized and traditional site based)	4.0	3.9	3.9	4.0	3.8	3.6
Customer relationship management technologies (e.g., automated text messages, emails to study participants)	3.9	3.9	3.7	3.8	3.8	3.8
E-consent technologies	3.7	3.8	3.7	3.8	3.8	3.7
Wearables/sensor data collection	3.7	3.7	3.5	3.7	3.8	3.8
Portals providing patient-facing information, i.e., consent documents, product candidate and trial information	3.6	3.7	3.6	3.7	3.8	3.7
Online patient communities	3.5	3.7	3.5	3.7	3.9	3.6
Electronic patient diaries	3.5	3.6	3.4	3.6	3.7	3.7
Completely site-less clinical trials	3.2	3.3	3.4	3.6	3.4	3.2

N: 46-51
Q: On a scale from 1 (substantial risk to participant diversity) to 5 (substantial benefit to participant diversity), how do you perceive each of the below to impact diversity in clinical research participation?

Community/Researcher Identity and Culture and Participant Diversity

Community/Researcher Identity and Culture and Participant Diversity

- On average, every executional tactic studied that related to *community/researcher identity and culture* was also perceived by respondents to have a positive impact on clinical trial participant diversity with respect to every demographic and disease-related variable.
- The tactics felt to have the most positive impacts were those in which advocacy for clinical research was brought directly into communities: community clinical research advocates across diverse populations, community interaction by healthcare providers, and use of trust bearers in the community to get messaging to patients and caregivers. These were felt to be particularly impactful when it came to racial and socioeconomic diversity.
- Diversity in sponsor/CRO/provider personnel and navigators provided by sponsors or sites were on average thought to be less, but still positively, impactful.

Community/Researcher Identity and Culture and Participant Diversity

On a scale from 1 (substantial risk to participant diversity) to 5 (substantial benefit to participant diversity), how do you perceive each of the below (executional tactics) to impact diversity in clinical research participation (with respect to each of the following demographic/disease variables)?

Mean Rating

Tactic \\ Demographic or Disease Variable	Race	Gender	Socio-economic	Rural vs. urban vs. suburban	Stage of patient journey	Global/ regional standards of care
Community clinical research advocates across diverse populations	4.5	4.3	4.4	4.2	3.8	3.8
Community interaction by healthcare providers	4.3	4.2	4.3	4.2	3.8	3.8
Diversity in clinical site personnel	4.2	4.0	3.8	3.8	3.4	3.6
Diversity in Sponsor/CRO/Provider personnel	3.8	3.6	3.3	3.4	3.3	3.6
Diversity-oriented advertising/recruitment campaigns	4.4	4.2	4.0	3.9	3.7	3.6
Navigators provided by Sponsors or sites	3.8	3.8	3.9	3.8	3.7	3.6
Positive attitude toward clinical research by primary healthcare providers	4.4	4.3	4.3	4.2	4.2	3.8
Use of trust bearers in the community to get messaging to patients and caregivers	4.5	4.1	4.4	4.2	3.9	3.7

N: 47-54
Q: On a scale from 1 (substantial risk to participant diversity) to 5 (substantial benefit to participant diversity), how do you perceive each of the below to impact diversity in clinical research participation?

Use of Artificial Intelligence (AI) in Protocol/Clinical Development Plan Design and Planning and Participant Diversity

Use of Artificial Intelligence and Participant Diversity

- On average, every executional tactic studied that related to *use of artificial intelligence (AI) in protocol/clinical development plan design and planning* was again perceived by respondents to have a positive impact on clinical trial participant diversity with respect to every demographic and disease-related variable.
- Application of AI to EHR (electronic health records) to identify eligibility criteria that impact diversity and to identify patient pathways that may enhance identification and enrollment of particular patient groups were thought to be most positively impactful, on average, when it came to racial and gender diversity.

Use of Artificial Intelligence (AI) in Protocol/Clinical Development Plan Design and Planning and Participant Diversity

On a scale from 1 (substantial risk to participant diversity) to 5 (substantial benefit to participant diversity), how do you perceive each of the below (executional tactics) to impact diversity in clinical research participation (with respect to each of the following demographic/disease variables)?

Mean Rating

Tactic \\ Demographic or Disease Variable	Race	Gender	Socio-economic	Rural vs. urban vs. suburban	Stage of patient journey	Global/ regional standards of care
Electronic Health Record (EHR) data to identify eligibility criteria that impact diversity	4.2	4.0	3.8	3.7	3.9	3.9
Electronic Health Record (EHR) data to identify patient pathways that may enhance identification and enrollment of particular (e.g., demographic) groups of patients	4.1	4.0	3.8	3.7	3.9	3.7
Electronic Health Record (EHR) data to model enrollment rate, site selection, country selection, clinical supply utilization	3.8	3.8	3.6	3.6	3.6	3.8
Electronic Health Record (EHR) data to understand procedures and schedules that would be least disruptive to standard of care	3.7	3.7	3.7	3.5	3.7	3.9

N: 45-50
Q: On a scale from 1 (substantial risk to participant diversity) to 5 (substantial benefit to participant diversity), how do you perceive each of the below to impact diversity in clinical research participation?

Use of Non-traditional Study Designs and Endpoints and Participant Diversity

Non-traditional Study Designs/Endpoints and Participant Diversity

- Finally, every executional tactic studied that related to *non-traditional study designs and endpoints* was also perceived by respondents to have a positive impact on clinical trial participant diversity with respect to every demographic and disease-related variable.
- By a margin, the tactic felt to have the most positive impact on every type of participant diversity was the use of observational studies using real world data. These were felt to be particularly impactful when it came to racial and socioeconomic diversity.
- In contrast, the use of novel digital endpoints was on average thought only to have a slightly positive impact on patient diversity.

Non-traditional Study Designs/Endpoints and Participant Diversity

On a scale from 1 (substantial risk to participant diversity) to 5 (substantial benefit to participant diversity), how do you perceive each of the below (executional tactics) to impact diversity in clinical research participation (with respect to each of the following demographic/disease variables)?

Mean Rating

Tactic \\ Demographic or Disease Variable	Race	Gender	Socio-economic	Rural vs. urban vs. suburban	Stage of patient journey	Global/ regional standards of care
Adaptive trials	3.8	3.8	3.7	3.7	3.8	3.7
Master/Platform/Umbrella/Basket protocols	3.7	3.7	3.6	3.6	3.8	3.7
Observational trials using Real World Data	4.2	4.1	4.0	4.0	4.2	4.0
Pragmatic trials	3.9	3.9	3.8	3.8	3.9	3.8
Precision medicine (using biomarkers, genomics)	3.9	4.0	3.7	3.6	3.9	3.7
Synthetic control arms	3.6	3.7	3.6	3.6	3.7	3.6
Use of novel Digital Endpoints	3.6	3.6	3.5	3.4	3.7	3.6

N: 45-49
Q: On a scale from 1 (substantial risk to participant diversity) to 5 (substantial benefit to participant diversity), how do you perceive each of the below to impact diversity in clinical research participation?

Thank You

Contact WCG Avoca:

(609) 252-9020

www.theavocagroup.com

179 Nassau Street, Suite 3A

Princeton, NJ 08542