OVERVIEW

Clinical trials have become increasingly global in scope. Some countries require testing of drugs in a country before they can be approved for sale in that country. Furthermore, as costs and regulations increase and patient recruitment becomes more difficult in the United States and Western Europe, those who run clinical trials look more to venues where these obstacles are less burdensome and recruitment more promising.

SCORR Marketing conducted a survey in partnership with Applied Clinical Trials to measure attitudes and beliefs of those in the health sciences as they pertain to the globalization of clinical trials. Specifically, this report seeks to identify the challenges faced in operating multiregion clinical trials and the difficulties inherent in setting standards in emerging markets.

The survey participants come from a variety of businesses — to name a few, contract research organizations, research sites and pharmaceutical companies — with departments or job titles spanning corporate management, research and development, and clinical research associates/coordinators. While a majority work for North American companies, almost one-third come from Europe.

In this report, we provide information about:

- Which factors push clinical trials out of the U.S. or Western Europe
- What reasons pull trials into specific countries or regions
- Countries/regions where clinical trial conduct is especially difficult and regions where conduct is most affordable
- Benefits gained by the communities that host trials
- Challenges faced by those who run multiregion clinical trials
- The importance of prioritizing and setting standards in emerging markets
- Predicted globalization trends
KEY RESULTS

Many issues make running multiregion clinical trials challenging, but regulatory issues are the most difficult.

When respondents were asked how difficult various issues were, they put regulatory issues at the top of the list. On a 1–5 scale (with 1 being the most difficult), regulatory issues (2.15) were viewed as more difficult than ethical (2.66), patient-specific (2.68) or even statistical (2.96) issues.

The biggest challenges overall

| Regulatory | 1st |
| Ethical | 2nd |
| Patient-specific | 3rd |
| Statistical | 4th |

This was true across all organization types, job functions and geographical regions.

- Among organization types, CROs find the most difficulty with regulatory issues (2.00).
- Among job functions, those in R&D positions view regulatory issues as most difficult (1.90).
- And among geographical regions, European respondents evaluate regulatory issues as being the most problematic (1.94).

Respondents then were asked what specific regulatory factor is the greatest obstacle to making multiregion trials work. In equal numbers, survey participants named “divergence in review and approval times across regions” (33%) and “lack of regulatory apparatus in some emerging markets” (also 33%).

The hardest specific obstacles

| Regulatory | 1. Divergence in review and approval times across regions |
| Patient-specific | 2. Standard of care differences |
| Ethical | 3. Clinical trial data transparency |
| Statistical | 4. Impact of regional differences |

Of patient-specific factors that pose the greatest challenge to screening patients while conducting multiregion trials, the standard of care differences (41%) obstacle was chosen most often followed by cultural differences (37%). CROs were most likely to select standard of care differences (73%), while research sites were most likely to select cultural differences (57%).

A plurality of respondents identified clinical trial data transparency (32%) as the ethical factor that poses the greatest impediment to conducting trials across regions. Research site survey participants were even more inclined to believe this (63%).

The impact of regional differences is the greatest statistical roadblock to these trials, according to nearly half (47%) of respondents. Consultants (63%), those in corporate management (58%) and respondents in North America companies (56%) were especially inclined to say this.
Setting standards in emerging markets is hard — and is especially difficult when it comes to investigator selection and training.

Survey participants evaluated the difficulty of setting standards in emerging markets in four areas: clinical supply chain, investigator selection and training, language (translation) and site selection. On a 1–5 scale (with 1 being the most difficult), the average rating for establishing standards for investigator selection and training (2.33) was lower than for clinical supply chain (2.43), site selection (2.61) or language (2.64). The fact that the highest rating (2.64) is well below 3.00 – the statistical average of a 1-5 scale – indicates that there are no areas in which standard-setting is considered an easy task.

The hardest areas in which to set standards

<table>
<thead>
<tr>
<th>Investigator selection and training</th>
<th>1st</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical supply chain</td>
<td>2nd</td>
</tr>
<tr>
<td>Site selection</td>
<td>3rd</td>
</tr>
<tr>
<td>Language (translation)</td>
<td>4th</td>
</tr>
</tbody>
</table>

What’s the most important factor to consider when selecting sites and investigators? Establishing good clinical practices (GCPs), said a plurality. R&D personnel were especially likely to say the establishment of GCPs is vital in the selection or training of investigators (80%), and in the selection of sites (70%).

Regarding clinical supply standards, respondents most often said that it is chiefly important to choose a location with an existing supply chain (39%). Corporate managers (64%) were especially inclined to emphasize the importance of using locations with supply chains already in place.

When language standards need to be established in emerging markets, survey participants were equally likely to select “choosing a location with existing qualified translators” (24%) and “developing qualified translators” (also 24%) as being most critical.

Factors that must be considered

<table>
<thead>
<tr>
<th>Issue</th>
<th>Factor Identified as Most Important</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigator selection and training</td>
<td>Establishing good clinical practices</td>
</tr>
<tr>
<td>Clinical supply chain</td>
<td>Choosing a location with an existing supply chain</td>
</tr>
<tr>
<td>Site selection</td>
<td>Establishing good clinical practices</td>
</tr>
<tr>
<td>Language (translation)</td>
<td>Choosing a location with existing qualified translators</td>
</tr>
<tr>
<td></td>
<td>Developing qualified translators</td>
</tr>
</tbody>
</table>
**KEY RESULTS (CONT)**

Gaining access to medicines is the biggest benefit realized by the communities that host global clinical trials, according to those who conduct the research.

Gaining access to medicines is what benefits host communities the most, respondents said, even more than development of health care infrastructure, exposure to external expertise, and the boost to the local economy. On a 1–5 scale (with 5 being the highest), the average rating for access to medicines (4.57) was higher than for development of health care infrastructure (4.29), exposure to external expertise (4.16) or the boost to the local economy (3.84).

<table>
<thead>
<tr>
<th>What most benefits host communities</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Access to medicines</td>
<td>1st</td>
</tr>
<tr>
<td>Development of health care infrastructure</td>
<td>2nd</td>
</tr>
<tr>
<td>Exposure to external expertise</td>
<td>3rd</td>
</tr>
<tr>
<td>Boost to the local economy</td>
<td>4th</td>
</tr>
</tbody>
</table>

This was true for most organizations:
- Consultants (4.75), sponsors (4.63) and CROs (4.45) each named access to medicines as being the biggest benefit.
- Respondents from research sites are the exception; they said being able to develop a health care infrastructure (4.75) is what benefits host communities the most.

Most job functions also selected access to medicines over other options:
- Project managers (5.00), clinical directors (4.67), R&D personnel (4.60) and corporate managers (4.58) identify access to medicines as the most important benefit.
- CRAs/CRCs value access to medicines as well as development of health care infrastructure (4.00 each).

Similarly, access to medicines has the highest average rating across geographic regions:
- Respondents from both Europe (4.63) and North America (4.59) prioritize access to medicines as an extremely important benefit to the communities that host global clinical trials.
- Those survey participants from outside of Europe and North America are just as likely to name access to medicines (4.33) as a benefit as exposure to external expertise (also 4.33).

On a side note, respondents from research sites and respondents who are clinical research associates or coordinators may be the ones most deeply involved on the ground in the host countries. It is interesting that both these groups indicated that gaining a health care infrastructure helps these communities the most.
**OTHER KEY TAKEAWAYS**

In which of the following countries/regions does your company currently conduct clinical trials?

Where are clinical trials most difficult; most affordable?

<table>
<thead>
<tr>
<th>Region</th>
<th>Most Difficult</th>
<th>Most Affordable</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America</td>
<td>39%</td>
<td>13%</td>
</tr>
<tr>
<td>Latin America</td>
<td>16%</td>
<td>26%</td>
</tr>
<tr>
<td>Western Europe</td>
<td>33%</td>
<td>15%</td>
</tr>
<tr>
<td>Russia / Eastern Europe</td>
<td>18%</td>
<td>47%</td>
</tr>
<tr>
<td>Middle East / North Africa</td>
<td>43%</td>
<td>19%</td>
</tr>
<tr>
<td>India</td>
<td>20%</td>
<td>60%</td>
</tr>
<tr>
<td>China</td>
<td>33%</td>
<td>38%</td>
</tr>
<tr>
<td>Other Asia</td>
<td>35%</td>
<td>21%</td>
</tr>
<tr>
<td>Australia</td>
<td>14%</td>
<td>11%</td>
</tr>
</tbody>
</table>

North America and Western Europe remain the most popular places for clinical trials, although North America — along with the Middle East/North Africa — is the region where conducting clinical trials is considered to be especially difficult. India and Russia/Eastern Europe are thought of as especially affordable places to conduct clinical trials.
OTHER KEY TAKEAWAYS (CONT)

How well these reasons explain why clinical trials are leaving the U.S. or Western Europe or moving into other regions

Exit from the U.S. and Western Europe

- Costs are too high: 3.81
- Difficulty recruiting patients: 3.60
- Lengthier timelines: 3.31
- Excessive regulations: 3.25

Move into certain countries/regions

- Costs are lower: 3.91
- Easier to recruit patients: 3.86
- Required testing in country before selling: 3.55
- Shorter timelines: 3.50

Costs are both the primary reason why clinical trials are moved out of North America and Western Europe and also why they are being pulled into other regions. Patient recruitment is the secondary reason.
Which of the following factors pose the greatest obstacle to conducting multiregion trials?

**Ethical factors**
- Clinical trial data transparency: 32%
- Health literacy of patients: 22%
- Informed consent of patients: 22%
- Rigorous assessment of adverse events: 22%
- Other: 4%

**Patient-specific factors**
- Standard of care differences: 41%
- Cultural differences: 37%
- Environmental differences: 14%
- Genetic/hereditary: 4%
- Other: 6%

**Regulatory factors**
- Divergence in review and approval times across regions: 33%
- Lack of regulatory apparatus in some emerging markets: 25%
- Harmonization of evidentiary requirements: 6%
- Differences in endpoints across regions: 33%
- Other: 4%

**Statistical factors**
- Impact of regional differences: 47%
- Methods for subgroup analysis: 18%
- Randomization issues: 16%
- Predefining regions: 14%
- Other: 4%

The impact of regional differences was not only the most cited statistical obstacle to conducting trials across regions, it was the most cited obstacle of any sort.
When it comes to selecting sites and investigators, making sure there are good clinical practice (GCP) standards set up is most critical. When considering the clinical supply chain, respondents said that choosing a place with an existing supply chain is most vital.
There is widespread belief that the trend toward globalization of clinical trials will continue. None of the survey respondents believe this trend will be reversed, and just 5 percent believe that it will be stalled.