Form Approved
OMB No. 0990-0421
Exp. Date 10/31/2020

INTRODUCTION

Thank you for logging on to this important HHS questionnaire. This questionnaire is being administered by HHS's contractor, Eastern Research Group, Inc. (ERG). Your responses and participation in this questionnaire are CONFIDENTIAL. ERG will compile the aggregated results; no individual responses will be identified to HHS.

The purpose of this questionnaire is to solicit information related to clinical trials (e.g., study costs, clinical trial times, likelihood of success) as well as your opinion on potential strategies that may help improve their efficiency. Your responses will help HHS assess:

- The most promising innovations and methods for clinical trial development,
- Barriers to the implementation of more efficient methods,
- Policy tools that can streamline clinical trials and their potential impact in reducing clinical trial costs and clinical trial times and/or improving likelihood of success, and
- Typical costs for novel drug, vaccine, and complex medical device clinical trials

The questionnaire should take 45 minutes or less of your time. The questionnaire software will save your responses as you move from page to page, so if you are interrupted, when you log in again you can start where you left off.

SCREENER FOR AREA OF EXPERTISE

1 Which type of clinical trials are you familiar with? *Please check all that apply*.

- ❒ Drugs, including biologics and therapeutic vaccines
- ❒ Preventive vaccines
- ❒ Complex medical devices – These include all devices that require FDA premarket approval (PMA).

Programmer Note 1. Depending which area(s) selected, display appropriate questions.

DRUG QUESTIONS

2 For each item listed below, please tell us if it is likely to have an impact on the cost of a clinical trial, cycle, clinical trial time, **OR** the likelihood that the study would be successful.

		Yes	No	Not sure
2.1	Mobile technologies	❍	❍	❍
2.2	Simplified clinical trial protocols and reduced amendments	❍	❍	❍
2.3	Reduced source data verification (SDV)	❍	❍	❍
2.4	Improvements in FDA review efficiency and interactions	❍	❍	❍
2.5	Staged approval	❍	❍	❍
2.6	Biomarkers as surrogate endpoints	❍	❍	❍
2.7	Electronic health records	❍	❍	❍
2.8	Patient registries	❍	❍	❍
2.9	Adaptive design	❍	❍	❍
2.10	Standardized contracts	❍	❍	❍

Programmer Note 2. If 2.1 = "Yes" then continue, otherwise go to Programmer Note 28. (i.e., continue for the next intervention with a "Yes" response).

Programmer Note 3. For Phase 3 in the table below, split into two phases, "Phase 3 – New Drugs" and "Phase 3- Label expansions" for the following interventions: 2.7 Electronic health records and 2.8 Patient registries. For all other interventions, only present a single "Phase 3."

3 For each of the clinical phases listed, please indicate whether the use of **mobile technologies** is likely to have an impact on the cost of a clinical trial study, clinical trial time, or the likelihood that the study would be successful. *Please check all that apply*.

	Phase	**Cost**	**Clinical Trial Time**	**Success Probability**	**N/A**
3.1	Pre-Clinical/Non-clinical Phase	❒	❒	❒	❒
3.2	Phase 1	❒	❒	❒	❒

3.3	Phase 2	❒	❒	❒	❒
3.4	Phase 3 – New Drugs	❒	❒	❒	❒
3.5	Phase 3- Label expansions	❒	❒	❒	❒
3.6	FDA NDA/BLA Phase	❒	❒	❒	❒
3.7	Phase 4	❒	❒	N/A	N/A

4 In your opinion, what is the expected change in percentage terms? Please note that the expected change could be negative or positive. For example, use of adaptive design in a Phase 3 study may increase the cost of the study by *x*% while reducing clinical trial time by *y*%.

Programmer Note 4. In 3.1, if Study cost = "TRUE OR Clinical Trial Time = TRUE OR Success Probability = TRUE, then continue, otherwise go to Programmer Note 8. (i.e., continue for the next phase with a box checked).

4.1 Pre-clinical/Non-clinical phase

		Expected Average Impact	Increase?	Decrease?
4.1.1	Study cost	_____%	❍	❍
4.1.2	Clinical trial time	_____%	❍	❍
4.1.3	Success probability	_____%	❍	❍

4.2 Please briefly explain your reasoning for the estimates you provided.

_____
_____
_____
_____

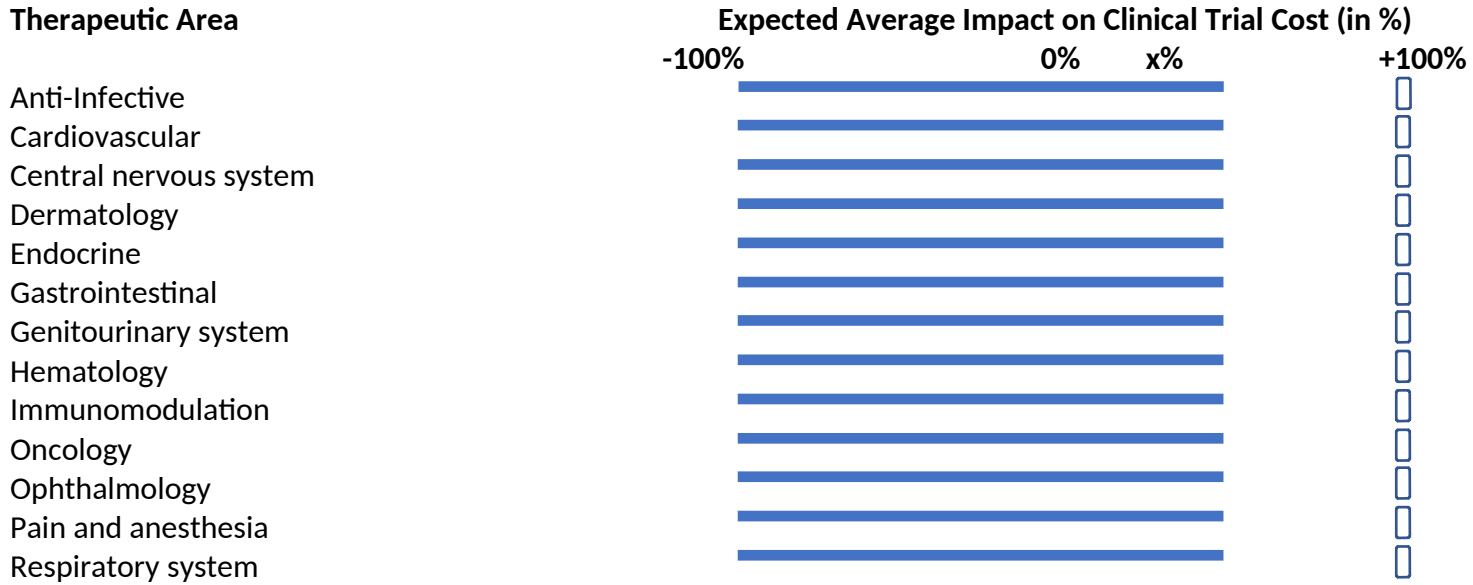
4.3 In your opinion, would the impacts you estimated above be expected to vary by therapeutic area?

❍ Yes
❍ No

❍ Not sure

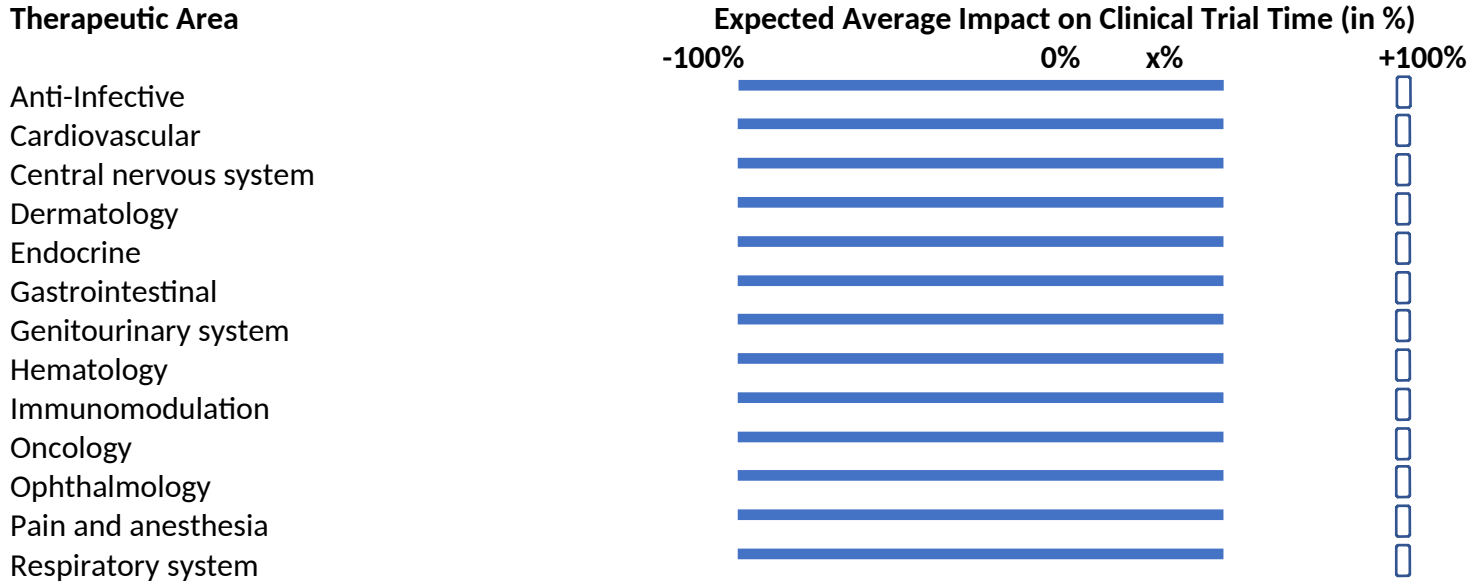
Programmer Note 5. If 4.3 = "Yes," AND 4.1.1 <> NULL AND 4.1.1 <> 0%, then continue, otherwise go to Programmer Note 6. (i.e., if Pre-Clinical/Non-clinical cost would vary by therapeutic area continue, otherwise go to clinical trial time) .

4.4 You estimated that the clinical trial study cost would on average [increase/decrease] by [x]% due to the use of **mobile technologies** above and that this would vary by therapeutic area. For each therapeutic area, please move the slider bar to reflect how the use of mobile technologies would impact costs for that therapeutic area. If you do not think there is a difference between the overall expected average impact [x]% you estimated and that for the listed therapeutic areas, please leave the estimate unchanged.



Programmer Note 6. If 4.3 = "Yes," AND 4.1.2<> NULL AND 4.1.2 <> 0%, then continue, otherwise go to Programmer Note 7. (i.e., if Pre-Clinical/Non-clinical clinical trial time would vary by therapeutic area continue, otherwise go to success probability).

4.5 You estimated that the clinical trial clinical trial time would on average [increase/decrease] by [x]% due to the use of **mobile technologies** above and that this would vary by therapeutic area. For each therapeutic area, please move the slider bar to reflect how the use of mobile technologies would impact clinical time for that therapeutic area. If you do not think there is a difference between the overall expected average impact [x]% you estimated and that for the listed therapeutic areas, please leave the estimate unchanged.



Programmer Note 7. If 4.3 = "Yes," AND 4.1.3 <> NULL AND 4.1.3 <> 0%, then continue, otherwise go to Programmer Note 8. (i.e., if Pre-Clinical/Non-clinical success probability would vary by therapeutic area continue, otherwise go to Phase 1).

4.6 You estimated that the clinical trial success probability would on average [increase/decrease] by [x]% due to the use of **mobile technologies** above and that this would vary by therapeutic area. For each therapeutic area, please move the slider bar to reflect how the use of mobile technologies would impact success probability for that therapeutic area. If you do not think there is a difference between the overall expected average impact [x]% you estimated and that for the listed therapeutic areas, please leave the estimate unchanged.

Therapeutic Area	Expected Average Impact on Clinical Trial Success Probability (in %)
	-100% 0% x% +100%
Anti-Infective	
Cardiovascular	
Central nervous system	
Dermatology	
Endocrine	
Gastrointestinal	
Genitourinary system	
Hematology	
Immunomodulation	
Oncology	
Ophthalmology	
Pain and anesthesia	
Respiratory system	

Programmer Note 8. In 3.2, if Study Cost = TRUE OR Clinical Trial Time = TRUE OR Success Probability = TRUE, then continue, otherwise go to Programmer Note 12. (i.e., if study cost, clinical trial time, or success probability would vary for Phase 1 continue, otherwise go to Phase 2).

4.7 Phase 1

		Estimated Impact	Increase?	Decrease?
4.7.1	Study cost	_____%	❍	❍
4.7.2	Clinical trial time	_____%	❍	❍
4.7.3	Success probability	_____%	❍	❍

4.8 Please briefly explain your reasoning for the estimates you provided.

_____

_____

_____

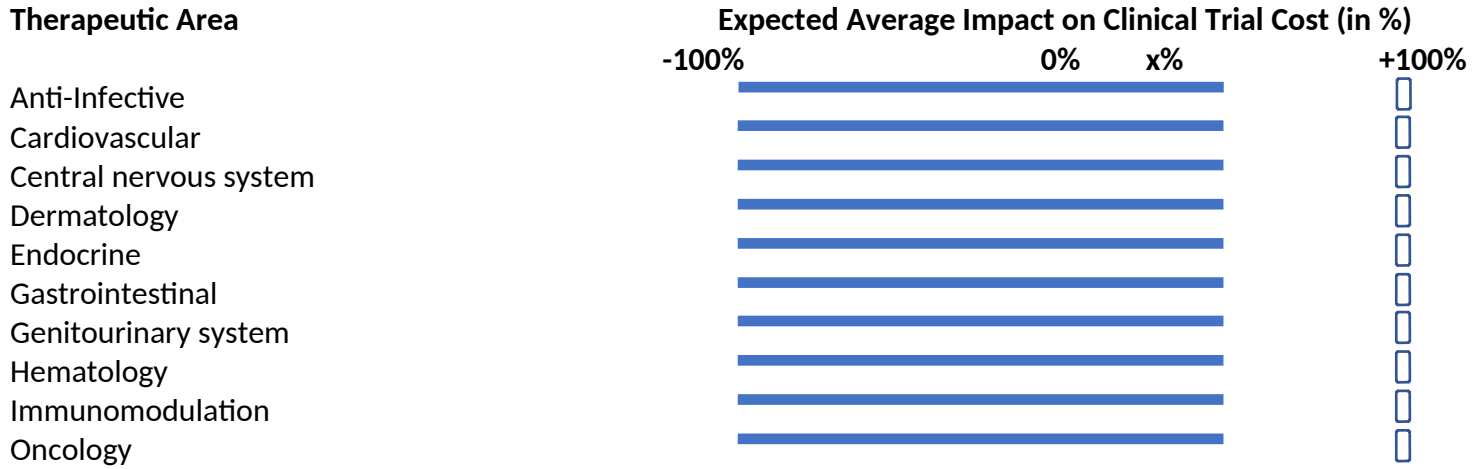
_____

4.9 In your opinion, do the impacts you estimated above are expected to vary by therapeutic area?

- ❍ Yes
- ❍ No
- ❍ Not sure

Programmer Note 9. If 4.9 = "Yes," AND 4.7.1 <> NULL AND 4.7.1 <> 0%, then continue, otherwise go to Programmer Note 10. (i.e., if Phase 1 cost would vary by therapeutic area continue, otherwise go to clinical trial time)..

4.10 You estimated that the clinical trial study cost would on average [increase/decrease] by [x]% due to the use of **mobile technologies** above and that this would vary by therapeutic area. For each therapeutic area, please move the slider bar to reflect how the use of mobile technologies would impact costs for that therapeutic area. If you do not think there is a difference between the overall expected average impact [x]% you estimated and that for the listed therapeutic areas, please leave the estimate unchanged.



Ophthalmology
Pain and anesthesia
Respiratory system

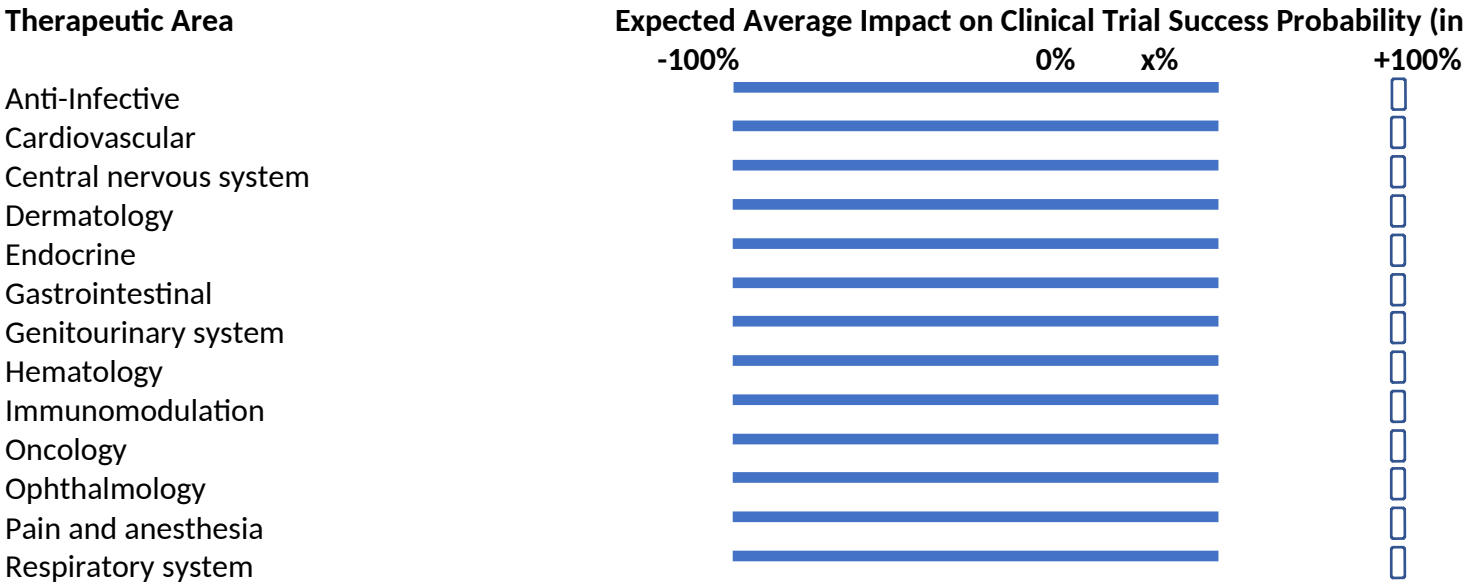
Programmer Note 10. If 4.9 = "Yes," AND 4.7.2 <> NULL AND 4.7.24.7.2 <> 0%, then continue, otherwise go to Programmer Note 11. (i.e., if Phase 1 clinical trial time would vary by therapeutic area continue, otherwise go to success probability).

4.11 You estimated that the clinical trial clinical trial time would on average [increase/decrease] by [x]% due to the use of **mobile technologies** above and that this would vary by therapeutic area. For each therapeutic area, please move the slider bar to reflect how the use of mobile technologies would impact clinical trial time for that therapeutic area. If you do not think there is a difference between the overall expected average impact [x]% you estimated and that for the listed therapeutic areas, please leave the estimate unchanged.

Therapeutic Area	**Expected Average Impact on Clinical Trial Time (in %)**
	-100% **0%** **x%** **+100%**
Anti-Infective	
Cardiovascular	
Central nervous system	
Dermatology	
Endocrine	
Gastrointestinal	
Genitourinary system	
Hematology	
Immunomodulation	
Oncology	
Ophthalmology	
Pain and anesthesia	
Respiratory system	

Programmer Note 11. If 4.9 = "Yes," AND 4.7.3 <> NULL AND 4.7.3 <> 0%, then continue, otherwise go to Programmer Note 12. (i.e., if Phase 1 success probability would vary by therapeutic area continue, otherwise go to Phase 2).

4.12 You estimated that the clinical trial success probability would on average [increase/decrease] by [x]% due to the use of **mobile technologies** above and that this would vary by therapeutic area. For each therapeutic area, please move the slider bar to reflect how the use of mobile technologies would impact success probability for that therapeutic area. If you do not think there is a difference between the overall expected average impact [x]% you estimated and that for the listed therapeutic areas, please leave the estimate unchanged.



Programmer Note 12. In 3.3, if Study cost = "TRUE OR Clinical Trial Time = TRUE OR Success Probability = TRUE, then continue, otherwise go to Programmer Note 16. (i.e., if study cost, clinical trial time, or success probability would vary for Phase 2 continue, otherwise go to Phase 3).

4.13 Phase 2

	Estimated Impact	Increase?	Decrease?
4.13.1 Study cost	_____%	❍	❍
4.13.2 Clinical trial time	_____%	❍	❍
4.13.3 Success probability	_____%	❍	❍

4.14 Please briefly explain your reasoning for the estimates you provided.

_____
_____
_____
_____

4.15 In your opinion, do the impacts you estimated above are expected to vary by therapeutic area?

❍ Yes
❍ No
❍ Not sure

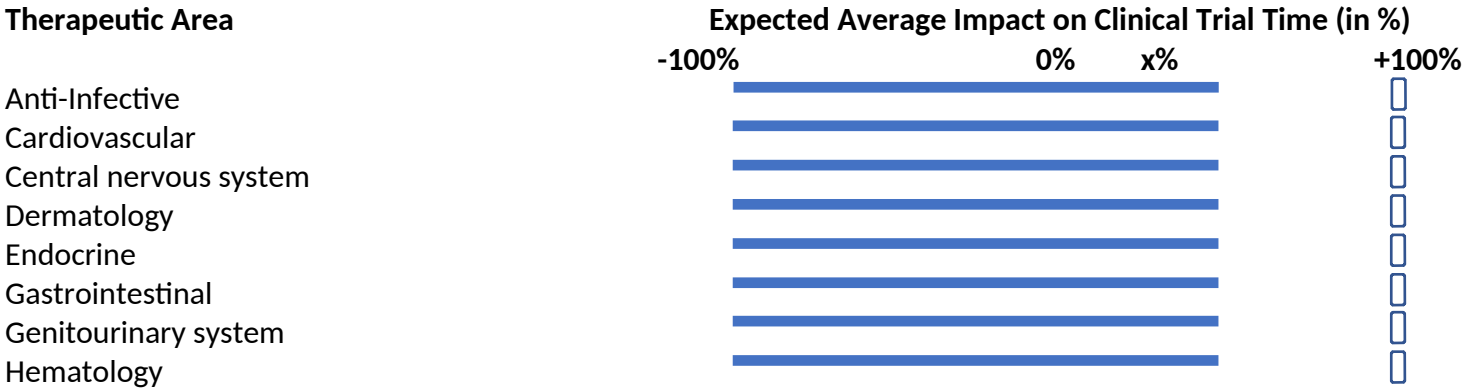
Programmer Note 13. If 4.15 = "Yes," AND 4.13.1 <> NULL AND 4.13.1 <> 0%, then continue, otherwise go to Programmer Note 14. (i.e., if Phase 2 cost would vary by therapeutic area continue, otherwise go to clinical trial time)..

4.16 You estimated that the clinical trial study cost would on average [increase/decrease] by [x]% due to the use of **mobile technologies** above and that this would vary by therapeutic area. For each therapeutic area, please move the slider bar to reflect how the use of mobile technologies would impact costs for that therapeutic area. If you do not think there is a difference between the overall expected average impact [x]% you estimated and that for the listed therapeutic areas, please leave the estimate unchanged.

Therapeutic Area	Expected Average Impact on Clinical Trial Cost (in %)
	-100% 0% x% +100%
Anti-Infective	
Cardiovascular	

Programmer Note 14. If 4.15 = "Yes," AND 4.13.2 <> NULL AND 4.13.2 <> 0%, then continue, otherwise go to Programmer Note 15. (i.e., if Phase 2 clinical trial time would vary by therapeutic area continue, otherwise go to success probability).

4.17 You estimated that the clinical trial clinical trial time would on average [increase/decrease] by [x]% due to the use of **mobile technologies** above and that this would vary by therapeutic area. For each therapeutic area, please move the slider bar to reflect how the use of mobile technologies would impact clinical trial time for that therapeutic area. If you do not think there is a difference between the overall expected average impact [x]% you estimated and that for the listed therapeutic areas, please leave the estimate unchanged.



Immunomodulation
Oncology
Ophthalmology
Pain and anesthesia
Respiratory system

Programmer Note 15. If 4.15 = "Yes," AND 4.13.3 <> NULL AND 4.13.3 <> 0%, then continue, otherwise go to Programmer Note 16. (i.e., if Phase 2 success probability would vary by therapeutic area continue, otherwise go to Phase 3).

4.18 You estimated that the clinical trial success probability would on average [increase/decrease] by [x]% due to the use of **mobile technologies** above and that this would vary by therapeutic area. For each therapeutic area, please move the slider bar to reflect how the use of mobile technologies would impact success probability for that therapeutic area. If you do not think there is a difference between the overall expected average impact [x]% you estimated and that for the listed therapeutic areas, please leave the estimate unchanged.

Therapeutic Area	**Expected Average Impact on Clinical Trial Success Probability (in %)**
	-100% **0%** **x%** **+100%**
Anti-Infective	
Cardiovascular	
Central nervous system	
Dermatology	
Endocrine	
Gastrointestinal	
Genitourinary system	
Hematology	
Immunomodulation	
Oncology	
Ophthalmology	
Pain and anesthesia	
Respiratory system	

Programmer Note 16. In 3.4, if Study Cost = "TRUE OR Clinical Trial Time = TRUE OR Success Probability = TRUE, then continue, otherwise go to Programmer Note 21. (i.e., if study cost, clinical trial time, or success probability would vary for Phase 3 continue, otherwise go to the FDA NDA/BLA Phase).

Programmer Note 17. For Phase 3, split into two phases for the following interventions: 2.7 Electronic health records and 2.8 Patient registries. For all other interventions, only present a single "Phase 3."

4.19 Phase 3

	Estimated Impact	Increase?	Decrease?
4.19.1 Study cost	_____%	❍	❍
4.19.2 Clinical trial time	_____%	❍	❍
4.19.3 Success probability	_____%	❍	❍

4.20 Please briefly explain your reasoning for the estimates you provided.

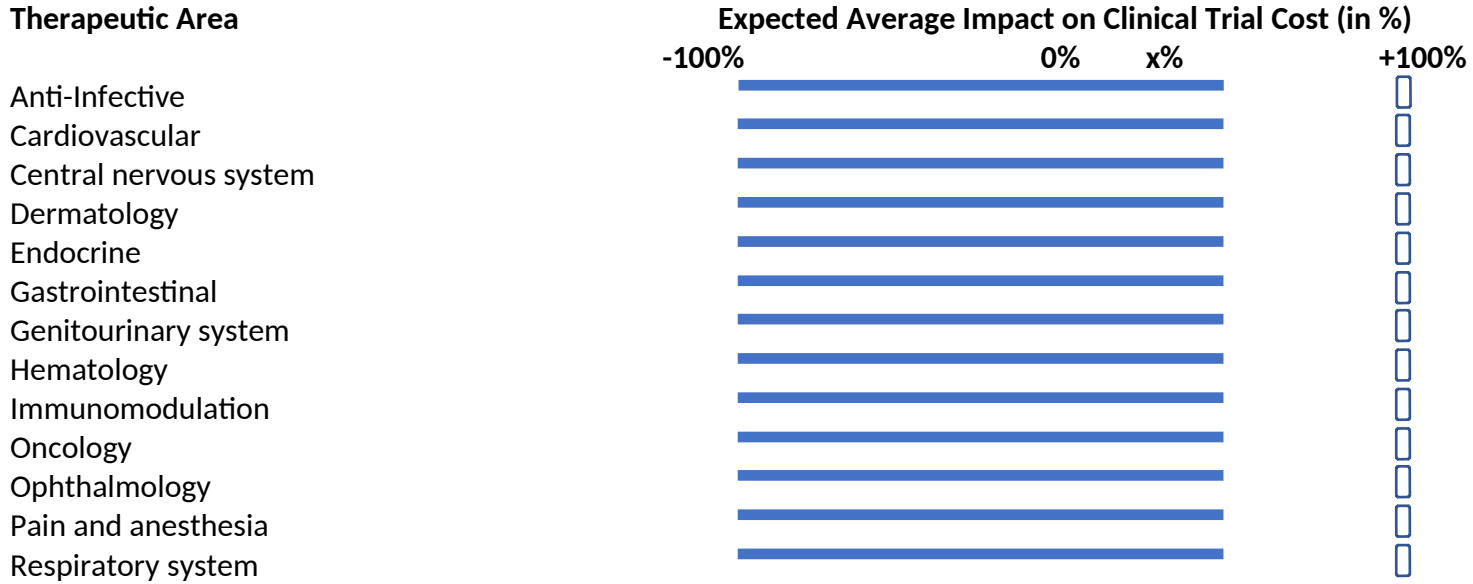
_____
_____
_____
_____

4.21 In your opinion, do the impacts you estimated above are expected to vary by therapeutic area?

❍ Yes
❍ No
❍ Not sure

Programmer Note 18. If 4.21 = "Yes," AND 4.19.1 <> NULL AND 4.19.1 <> 0%, then continue, otherwise go to Programmer Note 19. (i.e., if Phase 3 cost would vary by therapeutic area continue, otherwise go to clinical trial time).

4.22 You estimated that the clinical trial study cost would on average [increase/decrease] by [x]% due to the use of **mobile technologies** above and that this would vary by therapeutic area. For each therapeutic area, please move the slider bar to reflect how the use of mobile technologies would impact costs for that therapeutic area. If you do not think there is a difference between the overall expected average impact [x]% you estimated and that for the listed therapeutic areas, please leave the estimate unchanged.



Programmer Note 19. If 4.21 = "Yes," AND 4.19.2 <> NULL AND 4.19.2 <> 0%, then continue, otherwise go to Programmer Note 20. (i.e., if Phase 3 clinical trial time would vary by therapeutic area continue, otherwise go to success probability).

4.23 You estimated that the clinical trial clinical trial time would on average [increase/decrease] by [x]% due to the use of **mobile technologies** above and that this would vary by therapeutic area. For each therapeutic area, please move the slider bar to reflect how the use of mobile technologies would impact clinical trial time for that therapeutic area. If you do not think there is a difference between the overall expected average impact [x]% you estimated and that for the listed therapeutic areas, please leave the estimate unchanged.

Therapeutic Area	Expected Average Impact on Clinical Trial Time (in %)
	-100% 0% x% +100%
Anti-Infective	
Cardiovascular	
Central nervous system	
Dermatology	
Endocrine	
Gastrointestinal	
Genitourinary system	
Hematology	
Immunomodulation	
Oncology	
Ophthalmology	
Pain and anesthesia	
Respiratory system	

Programmer Note 20. If 4.21 = "Yes," AND 4.19.3 <> NULL AND 4.19.3 <> 0%, then continue, otherwise go to Programmer Note 21. (i.e., if Phase 3 success probability would vary by therapeutic area continue, otherwise go to the FDA NDA/BLA Phase).

4.24 You estimated that the clinical trial success probability would on average [increase/decrease] by [x]% due to the use of **mobile technologies** above and that this would vary by therapeutic area. For each therapeutic area, please move the slider bar to reflect how the use of mobile technologies would impact success probability for that therapeutic area. If you do not think there is a difference between the overall expected average impact [x]% you estimated and that for the listed therapeutic areas, please leave the estimate unchanged.

Therapeutic Area	Expected Average Impact on Clinical Trial Success Probability (in %)
	-100% 0% x% +100%
Anti-Infective	
Cardiovascular	
Central nervous system	

Dermatology
Endocrine
Gastrointestinal
Genitourinary system
Hematology
Immunomodulation
Oncology
Ophthalmology
Pain and anesthesia
Respiratory system

Programmer Note 21. In 3.6, if Study cost = "TRUE OR Clinical Trial Time = TRUE OR Success Probability = TRUE, then continue, otherwise go to Programmer Note 25. (i.e., if study cost, clinical trial time, or success probability would vary for the FDA NDA/BLA Phase continue, otherwise go to Phase 4).

4.25 FDA NDA/BLA phase

	Estimated Impact	Increase?	Decrease?
4.25.1 Study cost	_____%	❍	❍
4.25.2 Clinical trial time	_____%	❍	❍
4.25.3 Success probability	_____%	❍	❍

4.26 Please briefly explain your reasoning for the estimates you provided.

_____
_____
_____
_____

4.27 In your opinion, do the impacts you estimated above are expected to vary by therapeutic area?

- ❍ Yes
- ❍ No
- ❍ Not sure

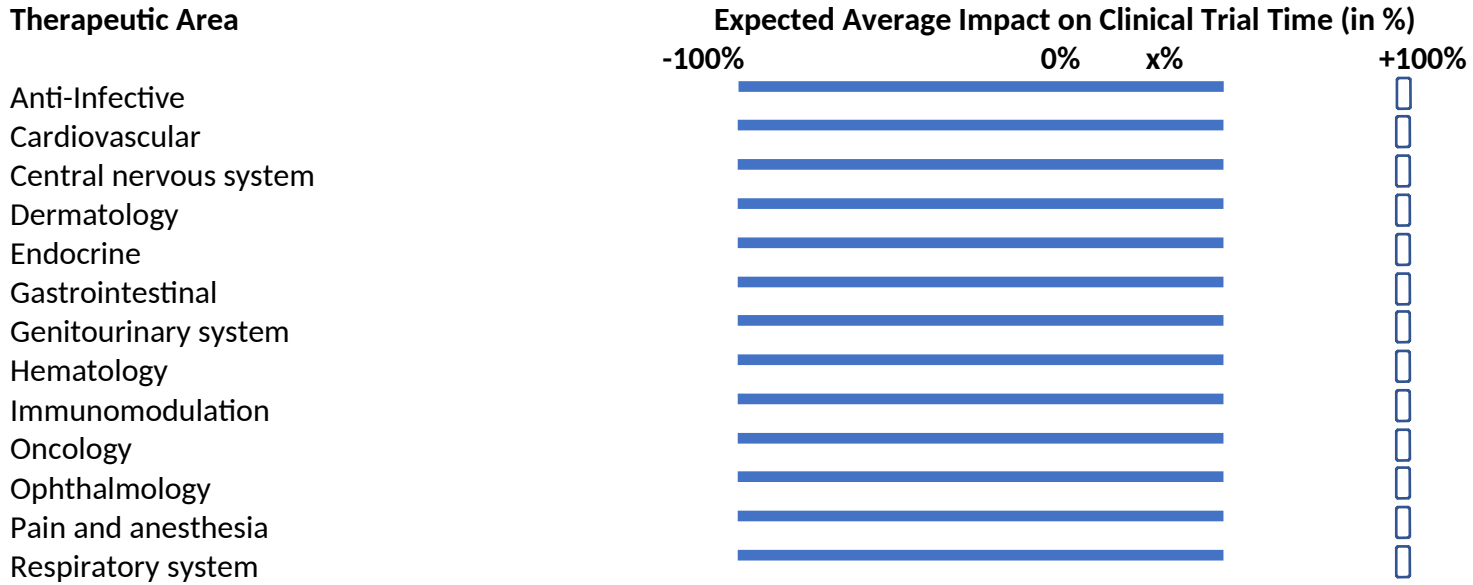
Programmer Note 22. If 4.27 = "Yes," AND 4.25.1 <> NULL AND 4.25.1 <> 0%, then continue, otherwise go to Programmer Note 23. (i.e., if the FDA NDA/BLA Phase cost would vary by therapeutic area continue, otherwise go to clinical trial time).

4.28 You estimated that the clinical trial study cost would on average [increase/decrease] by [x]% due to the use of **mobile technologies** above and that this would vary by therapeutic area. For each therapeutic area, please move the slider bar to reflect how the use of mobile technologies would impact costs for that therapeutic area. If you do not think there is a difference between the overall expected average impact [x]% you estimated and that for the listed therapeutic areas, please leave the estimate unchanged.

Therapeutic Area	**Expected Average Impact on Clinical Trial Cost (in %)**
	-100% **0%** **x%** **+100%**
Anti-Infective	
Cardiovascular	
Central nervous system	
Dermatology	
Endocrine	
Gastrointestinal	
Genitourinary system	
Hematology	
Immunomodulation	
Oncology	
Ophthalmology	
Pain and anesthesia	
Respiratory system	

Programmer Note 23. If 4.27 = "Yes," AND 4.25.2 <> NULL AND 4.25.2 <> 0%, then continue, otherwise go to Programmer Note 24. (i.e., if the FDA NDA/BLA Phase clinical trial time would vary by therapeutic area continue, otherwise go to success probability)Programmer Note 7..

4.29 You estimated that the clinical trial clinical trial time would on average [increase/decrease] by [x]% due to the use of **mobile technologies** above and that this would vary by therapeutic area. For each therapeutic area, please move the slider bar to reflect how the use of mobile technologies would impact clinical trial time for that therapeutic area. If you do not think there is a difference between the overall expected average impact [x]% you estimated and that for the listed therapeutic areas, please leave the estimate unchanged.



Programmer Note 24. If 4.27 = "Yes," AND 4.25.3 <> NULL AND 4.25.3 <> 0%, then continue, otherwise go to Programmer Note 25. (i.e., if the FDA NDA/BLA Phase success probability would vary by therapeutic area continue, otherwise go to Phase 4).

4.30 You estimated that the clinical trial success probability would on average [increase/decrease] by [x]% due to the use of **mobile technologies** above and that this would vary by therapeutic area. For each therapeutic area, please move the slider bar to reflect how the use of mobile technologies would impact success probability for that therapeutic area. If you do not think there is a difference between the overall expected average impact [x]% you estimated and that for the listed therapeutic areas, please leave the estimate unchanged.

Therapeutic Area	**Expected Average Impact on Clinical Trial Success Probability (in %)**
	-100% **0%** **x%** **+100%**
Anti-Infective	
Cardiovascular	
Central nervous system	
Dermatology	
Endocrine	
Gastrointestinal	
Genitourinary system	
Hematology	
Immunomodulation	
Oncology	
Ophthalmology	
Pain and anesthesia	
Respiratory system	

Programmer Note 25. In 3.7, if Study cost = "TRUE OR Clinical Trial Time = TRUE OR Success Probability = TRUE, then continue, otherwise go to Programmer Note 28. (i.e., if study cost, clinical trial time, or success probability would vary for Phase 4 continue, otherwise go to the next intervention).

4.31 Phase 4

Estimated Impact	**Increase?**	**Decrease?**

4.31.1 Study cost	_____%	❍	❍
4.31.2 Clinical trial time	_____%	❍	❍

4.32 Please briefly explain your reasoning for the estimates you provided.

_____
_____
_____
_____

4.33 In your opinion, do the impacts you estimated above are expected to vary by therapeutic area?

❍ Yes
❍ No
❍ Not sure

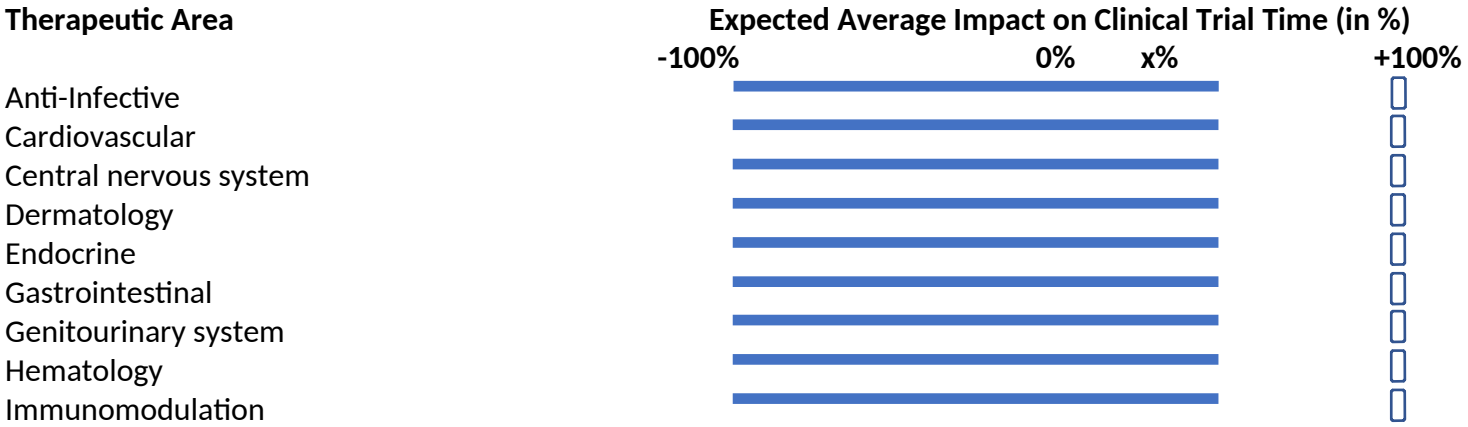
Programmer Note 26. If 4.33 = "Yes," AND 4.31.1 <> NULL AND 4.31.1 <> 0%, then continue, otherwise go to Programmer Note 27. (i.e., if Phase 4 cost would vary by therapeutic area continue, otherwise go to clinical trial time).

4.34 You estimated that the clinical trial study cost would on average [increase/decrease] by [x]% due to the use of **mobile technologies** above and that this would vary by therapeutic area. For each therapeutic area, please move the slider bar to reflect how the use of mobile technologies would impact costs for that therapeutic area. If you do not think there is a difference between the overall expected average impact [x]% you estimated and that for the listed therapeutic areas, please leave the estimate unchanged.

Therapeutic Area	**Expected Average Impact on Clinical Trial Cost (in %)**
	-100% **0%** **x%** **+100%**
Anti-Infective	
Cardiovascular	
Central nervous system	
Dermatology	

Programmer Note 27. If 4.33 = "Yes," AND 4.31.2 <> NULL AND 4.31.2 <> 0%, then continue, otherwise go to Programmer Note 28. (i.e., if Phase 4 clinical trial time would vary by therapeutic area continue, otherwise go to the next intervention).

4.35 You estimated that the clinical trial clinical trial time would on average [increase/decrease] by [x]% due to the use of **mobile technologies** above and that this would vary by therapeutic area. For each therapeutic area, please move the slider bar to reflect how the use of mobile technologies would impact clinical trial time for that therapeutic area. If you do not think there is a difference between the overall expected average impact [x]% you estimated and that for the listed therapeutic areas, please leave the estimate unchanged.



Oncology
Ophthalmology
Pain and anesthesia
Respiratory system

Programmer Note 28. Go to next intervention in Question 2 and cycle through Questions 3 and 4.

VACCINE QUESTIONS

5 We are interested in better characterizing the costs of clinical trials for new vaccines at a granular level, if possible. Please provide your best estimate for each of the clinical trial elements noted below. You may choose to provide a single estimate that in your opinion represents the average or a range (e.g., a lower and an upper bound).

		Phase 1	Phase 2	Phase 3	Phase 4
Per Study	Data collection, management, and analysis	_____	_____	_____	_____
	Number of IRB approvals	_____	_____	_____	_____
	Number of sites	_____	_____	_____	_____
Per Site	Site recruitment cost	_____	_____	_____	_____
	Site retention cost	_____	_____	_____	_____
	Number of patients	_____	_____	_____	_____
Per Patient	Patient recruitment cost	_____	_____	_____	_____
	Patient retention cost	_____	_____	_____	_____
	RN/CRA cost	_____	_____	_____	_____
	Physician cost	_____	_____	_____	_____
	Clinical procedure cost	_____	_____	_____	_____
	Central laboratory cost	_____	_____	_____	_____

6 We are interested in better characterizing the duration of each phase of clinical trials for new vaccines. For each phase, please give your best estimate of the average cycle time, in months.

Phase	Average Clinical Trial Time (in months)

Pre-clinical/Non-clinical	_____ months
Phase 1	_____ months
Phase 2	_____ months
Phase 3	_____ months
FDA BLA Phase	_____ months
Phase 4	_____ months

7 We are interested in better characterizing the probability of success of each phase of clinical trials for new preventive vaccines. For each phase, please give your best estimate of the average likelihood a vaccine will move to the next phase.

Phase	**Average Likelihood of Success (in %)**
Pre-clinical/Non-clinical to Phase 1	_____ %
Phase 1 to Phase 2	_____ %
Phase 2 to Phase 3	_____ %
Phase 3 to FDA BLA Phase	_____ %
FDA BLA to Market	_____ %

8 We are also interested in characterizing the effect of several policy interventions on preventive vaccine clinical trials. For each item listed below, please tell us if it is likely to have an impact on the cost of a clinical trial study, clinical trial time, **OR** the likelihood that the study would be successful.

		Yes	**No**	**Not sure**
8.1	Mobile technologies	❍	❍	❍
8.2	Simplified clinical trial protocols and reduced amendments	❍	❍	❍
8.3	Reduced source data verification (SDV)	❍	❍	❍
8.4	Improvements in FDA review efficiency and interactions	❍	❍	❍
8.5	Staged approval	❍	❍	❍
8.6	Biomarkers as surrogate endpoints	❍	❍	❍
8.7	Electronic health records	❍	❍	❍
8.8	Patient registries	❍	❍	❍

8.9	Adaptive design	❍	❍	❍
8.10	Standardized contracts	❍	❍	❍
8.11	CDC/NIH developing epidemiological data on disease incidence	❍	❍	❍
8.12	Federally supported cGMP-compliant manufacturing facilities	❍	❍	❍

Programmer Note 29. If 8.1 = "Yes" then continue, otherwise go to Programmer Note 36. (i.e., continue for the next intervention with a "Yes" response).

9 For each of the clinical phases listed, please indicate whether the use of **mobile technologies** is likely to have an impact on the cost of a clinical trial study, clinical trial time, or the likelihood that the study would be successful. *Please check all that apply*.

	Phase	**Cost**	**Clinical Trial Time**	**Success Probability**	**N/A**
9.1	Pre-Clinical/Non-clinical Phase	❒	❒	❒	❒
9.2	Phase 1	❒	❒	❒	❒
9.3	Phase 2	❒	❒	❒	❒
9.4	Phase 3	❒	❒	❒	❒
9.5	FDA NDA/BLA Phase	❒	❒	❒	❒
9.6	Phase 4	❒	❒	N/A	N/A

10 In your opinion, what is the expected change in percentage terms? Please note that the expected change could be negative or positive. For example, use of adaptive design in a Phase 3 study may increase the cost of the study by *x*% while reducing clinical trial time by *y*%.

Programmer Note 30. In 9.1, if Study cost = "TRUE OR Clinical Trial Time = TRUE OR Success Probability = TRUE, then continue, otherwise go to Programmer Note 31. (i.e., if Pre-Clinical/Non-clinical study cost, clinical trial time, or success probability would vary continue, otherwise go to Phase 1).

10.1 Pre-clinical/Non-clinical phase

	Expected Average Impact	Increase?	Decrease?
10.1.1 Study cost	_____%	❍	❍
10.1.2 Clinical trial time	_____%	❍	❍
10.1.3 Success probability	_____%	❍	❍

10.2 Please briefly explain your reasoning for the estimates you provided.

_____
_____
_____
_____

Programmer Note 31. In 9.2 if Study cost = "TRUE OR Clinical Trial Time = TRUE OR Success Probability = TRUE, then continue, otherwise go to Programmer Note 32. (i.e., if study cost, clinical trial time, or success probability would vary for Phase 1 continue, otherwise go to Phase 2).

10.3 Phase 1

	Estimated Impact	Increase?	Decrease?
10.3.1 Study cost	_____%	❍	❍
10.3.2 Clinical trial time	_____%	❍	❍
10.3.3 Success probability	_____%	❍	❍

10.4 Please briefly explain your reasoning for the estimates you provided.

_____
_____
_____
_____

Programmer Note 32. In 9.3, if Study cost = "TRUE OR Clinical Trial Time = TRUE OR Success Probability = TRUE, then continue, otherwise go to Programmer Note 33. (i.e., if study cost, clinical trial time, or success probability would vary for Phase 2 continue, otherwise go to Phase 3).

10.5 Phase 2

	Estimated Impact	Increase?	Decrease?
10.5.1 Study cost	_____%	❍	❍
10.5.2 Clinical trial time	_____%	❍	❍
10.5.3 Success probability	_____%	❍	❍

10.6 Please briefly explain your reasoning for the estimates you provided.

_____
_____
_____
_____

Programmer Note 33. In 9.4, if Study cost = "TRUE OR Clinical Trial Time = TRUE OR Success Probability = TRUE, then continue, otherwise go to Programmer Note 34. (i.e., if study cost, clinical trial time, or success probability would vary for Phase 3 continue, otherwise go to the FDA BLA phase).

10.7 Phase 3

	Estimated Impact	Increase?	Decrease?
10.7.1 Study cost	_____%	❍	❍
10.7.2 Clinical trial time	_____%	❍	❍
10.7.3 Success probability	_____%	❍	❍

10.8 Please briefly explain your reasoning for the estimates you provided.

_____
_____
_____
_____

Programmer Note 34. In 9.5, if Study cost = "TRUE OR Clinical Trial Time = TRUE OR Success Probability = TRUE, then continue, otherwise go to Programmer Note 35. (i.e., if study cost, clinical trial time, or success probability would vary for the FDA BLA phase continue, otherwise go to Phase 4)

10.9 FDA BLA phase

	Estimated Impact	Increase?	Decrease?
10.9.1 Study cost	_____%	❍	❍
10.9.2 Clinical trial time	_____%	❍	❍
10.9.3 Success probability	_____%	❍	❍

10.10 Please briefly explain your reasoning for the estimates you provided.

_____
_____
_____
_____

Programmer Note 35. In 9.6, if Study cost = "TRUE OR Clinical Trial Time = TRUE OR Success Probability = TRUE, then continue, otherwise go to Programmer Note 36. (i.e., if study cost, clinical trial time, or success probability would vary for Phase 4 continue, otherwise go to the next intervention.

10.11 Phase 4

	Estimated Impact	Increase?	Decrease?

10.11.1	Study cost	_____%	❍	❍
10.11.2	Clinical trial time	_____%	❍	❍

10.12 Please briefly explain your reasoning for the estimates you provided.

_____
_____
_____
_____

Programmer Note 36. Go to next intervention in Question 8 and cycle through Questions 9 and 10.

COMPLEX MEDICAL DEVICE QUESTIONS

11 We are interested in better characterizing the costs of clinical trials for new complex medical devices (i.e., devices that require FDA premarket approval) at a granular level, if possible. Please provide your best estimate for each of the clinical trial elements noted below. You may choose to provide a single estimate that in your opinion represents the average or a range (e.g., a lower and an upper bound).

		Pilot Study Phase	Pivotal Study Phase	FDA PMA Phase	Post-approval Study Phase
Per Study	Data collection, management, and analysis	_____	_____	_____	_____
	Number of IRB approvals	_____	_____	_____	_____
	Number of sites	_____	_____	_____	_____
Per Site	Site recruitment cost	_____	_____	_____	_____
	Site retention cost	_____	_____	_____	_____
	Number of patients	_____	_____	_____	_____
Per Patient	Patient recruitment cost	_____	_____	_____	_____
	Patient retention cost	_____	_____	_____	_____
	RN/CRA cost	_____	_____	_____	_____

Physician cost	_____	_____	_____	_____
Clinical procedure cost	_____	_____	_____	_____
Central laboratory cost	_____	_____	_____	_____

12 We are interested in better characterizing the total duration of each phase of clinical trials for new complex medical devices. For each phase, please give your best estimate of the average clinical trial time, in months.

Phase	**Average Clinical Trial Time (in months)**
Pre-Clinical/Non-clinical Phase	_____ months
Pilot Study	_____ months
Pivotal Study Phase	_____ months
FDA PMA Phase	_____ months
Post-approval Study Phase	_____ months

13 We are interested in better characterizing the probability of success of each phase of clinical trials for new complex medical devices. For each phase, please give your best estimate of the average likelihood a complex medical device will go to the next phase.

Phase	**Average Likelihood of Success (in %)**
Pre-Clinical/Non-clinical to Pilot Phase	_____ %
Pilot Phase to Pivotal Phase	_____ %
Pivotal Phase to FDA PMA Phase	_____ %
FDA PMA Phase to Market	_____ %

14 We are also interested in characterizing the effect of several policy interventions on complex medical device clinical trials. For each item listed below, please tell us if it is likely to have an impact on the cost of a clinical trial study, clinical trial time, **OR** the likelihood that the study would be successful.

		Yes	No	Not sure
14.1	Mobile technologies	❍	❍	❍
14.2	Simplified clinical trial protocols and reduced amendments	❍	❍	❍
14.3	Reduced source data verification (SDV)	❍	❍	❍
14.4	Improvements in FDA review efficiency and interactions	❍	❍	❍
14.5	Staged approval	❍	❍	❍
14.6	Biomarkers as surrogate endpoints	❍	❍	❍
14.7	Electronic health records	❍	❍	❍
14.8	Patient registries	❍	❍	❍
14.9	Adaptive design	❍	❍	❍
14.10	Standardized contracts	❍	❍	❍
14.11	Encouraging the use of centralized IRBs	❍	❍	❍

Programmer Note 37. If 14.1 = "Yes" then continue, otherwise go to Programmer Note 43. (i.e., continue for the next intervention with a "Yes" response).

15 For each of the clinical phases listed, please indicate whether the use of **mobile technologies** is likely to have an impact on the cost of a clinical trial study, clinical trial time, or the likelihood that the study would be successful. *Please check all that apply*.

Phase		**Cost**	**Clinical Trial Time**	**Success Probability**	**N/A**
15.1	Pre-clinical/Non-clinical Phase	❒	❒	❒	❒
15.2	Pilot Study	❒	❒	❒	❒
15.3	Pivotal Study Phase	❒	❒	❒	❒
15.4	FDA PMA Phase	❒	❒	❒	❒
15.5	Post-approval Study Phase	❒	❒	N/A	N/A

16 In your opinion, what is the expected change in percentage terms? Please note that the expected change could be negative or positive. For example, use of adaptive design in a pilot study may increase the cost of the study by *x*% while reducing clinical trial time by *y*%.

Programmer Note 38. In 15.1, if Study cost = "TRUE OR Clinical Trial Time = TRUE OR Success Probability = TRUE, then continue, otherwise go to Programmer Note 39. (i.e., if Pre-Clinical/Non-clinical study cost, clinical trial time, or success probability would vary continue, otherwise go to the Pilot Study phase).

16.1 Pre-Clinical/Non-clinical phase

	Expected Average Impact	Increase?	Decrease?
16.1.1 Study cost	_____%	❍	❍
16.1.2 Clinical trial time	_____%	❍	❍
16.1.3 Success probability	_____%	❍	❍

16.2 Please briefly explain your reasoning for the estimates you provided.

_____
_____
_____
_____

Programmer Note 39. In 15.2, if Study cost = "TRUE OR Clinical Trial Time = TRUE OR Success Probability = TRUE, then continue, otherwise go to Programmer Note 40. (i.e., if Pilot Study cost, clinical trial time, or success probability would vary continue, otherwise go to the Pivotal phase).

16.3 Pilot study phase

	Estimated Impact	Increase?	Decrease?
16.3.1 Study cost	_____%	❍	❍
16.3.2 Clinical trial time	_____%	❍	❍
16.3.3 Success probability	_____%	❍	❍

16.4 Please briefly explain your reasoning for the estimates you provided.

_____
_____
_____
_____

Programmer Note 40. In 15.3, if Study cost = "TRUE OR Clinical Trial Time = TRUE OR Success Probability = TRUE, then continue, otherwise go to Programmer Note 41. (i.e., if Pivotal Study cost, clinical trial time, or success probability would vary continue, otherwise go to the FDA PMA phase).

16.5 Pivotal study phase

	Estimated Impact	Increase?	Decrease?
16.5.1 Study cost	_____%	❍	❍
16.5.2 Clinical trial time	_____%	❍	❍
16.5.3 Success probability	_____%	❍	❍

16.6 Please briefly explain your reasoning for the estimates you provided.

_____
_____
_____
_____

Programmer Note 41. In 15.4 if Study cost = "TRUE OR Clinical Trial Time = TRUE OR Success Probability = TRUE, then continue, otherwise go to Programmer Note 42. (i.e., if FDA PMA cost, clinical trial time, or success probability would vary continue, otherwise go to the post-approval phase).

16.7 FDA PMA Phase

	Estimated Impact	Increase?	Decrease?
16.7.1 Study cost	_____%	❍	❍
16.7.2 Clinical trial time	_____%	❍	❍
16.7.3 Success probability	_____%	❍	❍

16.8 Please briefly explain your reasoning for the estimates you provided.

_____
_____
_____
_____

Programmer Note 42. In 15.5, if Study cost = "TRUE OR Clinical Trial Time = TRUE OR Success Probability = TRUE, then continue, otherwise go to Programmer Note 43. (i.e., if post-approval cost, clinical trial time, or success probability would vary continue, otherwise go to the next intervention).

16.9 Post-approval study phase

	Estimated Impact	Increase?	Decrease?
16.9.1 Study cost	_____%	❍	❍
16.9.2 Clinical trial time	_____%	❍	❍

16.10 Please briefly explain your reasoning for the estimates you provided.

_____

_____

_____

_____

Programmer Note 43. Go to next intervention in Question 14 and cycle through Questions 15 and 16.

END

Thank you for responding to our questions.

MOUSE-OVER DEFINITIONS

Programmer Note 44. Provide definitions that appear when the respondent hovers over "cost," "clinical trial time," and "success probability," as follows:

- **Cost:** Estimated average total cost of clinical trial phase.
- **Clinical Trial Time:** The time for each phase, from inception to the completion of the study report for that phase.
- **Success Probability:** The probability of successful transition to the next trial phase, i.e., phase transition probability.
    - **For Pre-clinical/Non-clinical Phase box:** From Pre-clinical/Non-clinical Phase to Phase 1.
    - **For Phase 1 box:** From Phase 1 to Phase 2.
    - **For Phase 2 box:** From Phase 2 to Phase 3.
    - **For Phase 3 box:** From Phase 3 to FDA/BLA submission for review.
    - **For FDA NDA/BLA Phase box:** From FDA/BLA submission to approval.

Programmer Note 45. Provide definitions that appear when the respondent hovers over each intervention, as follows:

Mobile technologies: Mobile technologies can include cell phones, wearable trackers, and other devices that capture data directly from patients. Electronic data capture means capturing study data in electronic format. A policy intervention could include encouraging the use of mobile and other technologies in clinical trials and the development process as a whole, and clarifying requirements around their use.

Simplified clinical trial protocols and reduced amendments: Intervention elements could include encouraging sponsors to simplify clinical trial protocols, where possible, ensuring that they have a clear understanding of what is required by FDA and what is superfluous

Reduced source data verification (SDV): Source data verification is the process of comparing data collected throughout the clinical trial to the original source of information as to verify data integrity. A policy intervention could include engaging sponsors in discussions on the topic of data and site monitoring to ensure that they are aware of the FDA guidance stating that 100 percent source data verification is not required, as well as continuing to educate reviewers on this policy.

Improvements in FDA review efficiency and interactions: A policy intervention could include providing more opportunity to identify, discuss, and resolve substantive issues during the review, continuing to educate FDA reviewers on changes in FDA policy, and providing more transparency about what endpoints are required.

Staged approval: Staged approval could entail granting provisional marketing approval to market a drug/device/vaccine after safety and basic efficacy have been shown, and then continuing to collect additional safety and efficacy data. This would reduce the threshold for initial approval, perhaps with a limited patient population, and then gradually expand it as more data are collected.

Biomarkers as surrogate endpoints: Biomarkers as surrogate endpoints are biological indicators that may correlate with the desired clinical endpoint, for example when it would take a long time for the clinical endpoint to become evident. Policy interventions could entail clarifying the path to biomarker validation or encouraging collaboration between academics, public entities, and industry to develop and validate biomarkers for use as surrogate endpoints.

Electronic health records: EHRs, used here as being synonymous with electronic medical records (EMRs), are digital versions of the data collected when a patient visits a healthcare provider's office. A policy intervention could entail encouraging sponsors to use EHRs for patient and physician recruitment or to collect clinical endpoints.

Patient registries: A patient registry is an organized system that uses observational study methods to collect uniform data to evaluate specified outcomes of a disease or condition for a population. Registries include those established by a patient organization for a particular disease as well as registries that are sometimes established by the manufactured and used as a postmarketing study. Policy interventions could entail encouraging sponsors to use registry data for patient and physician recruitment or to collect clinical endpoints.

Adaptive design: An adaptive design allows modifications to the trial and/or statistical procedures of the trial after its initiation without undermining its validity and integrity. Policy interventions could include clarifying FDA's policies on whether certain types of adaptive trial design are acceptable and encouraging their use.

Standardized contracts: Standardized contracts are contract templates for use in sponsor-initiated multi-site trials, intended to reduce the complexity and duration of contract negotiations for clinical trial studies. Policy interventions could entail encouraging the use of master contracts and standardized contracts or compiling existing resources into a central location.

[*Devices only*] **Encouraging the use of centralized IRBs**: A centralized Institutional Review Board is a single IRB of record for all clinical trial sites in a multi-center trial, which would remove the need to obtain approvals from multiple local IRBs. Policy interventions could entail creating guidance or other educational material, and encouraging local IRBs not to require local IRB approval.

[*Vaccines only*] **CDC/NIH developing epidemiological data on disease incidence**: This intervention would entail CDC and/or NIH collecting epidemiological data on disease incidence that is tailored to developing vaccines, rather than each vaccine manufacturer collecting it individually.

[*Vaccines only*] **Federally supported cGMP-compliant manufacturing facilities**: This policy intervention would include providing additional funding or other support to help increase the number/capacity of cGMP-compliant manufacturing facilities that can produce batches of vaccines for use in clinical trial studies.