Appendix 1: Survey Tool

Thank you for participating in this survey. We aim to describe the implications of current policies on the future biotechnology innovation ecosystem and patient care. We value your insights regarding the potential effects of these policies and help inform policymakers.

This survey should require only **5-10 minutes to complete**. Your responses will be anonymized and only presented in aggregate form, with no individual attribution. For open-ended questions, we request that you do not provide any personally identifiable information. In the event that such information is inadvertently included, it will be removed from the data before any analysis takes place.

Please download and review the Informed Consent Form here before proceeding. If you have questions, you may contact Erika Modina at emodina@stanford.edu.

By selecting the "I voluntarily consent to participate in this survey" option below, you are giving your consent to participate in the survey.

Informed Consent

a) I voluntarily consent to participate in this survey.
b) I decline to participate in this survey. *(respondents exit survey if they decline to participate)*

Which role in biotechnology best describes you? Choose only one.

a) Healthcare investor
b) Innovator or Biotech Leader
c) Neither (*respondents exit survey if neither is selected*)

Demographic Data (Investors)

What type of biotech investor are you? Please select the option that best represents your profile

a) Private equity or venture capital
b) Angel investor or family office
c) Others. Please specify:

How much of your current fund is allocated to biotech?

a) < $10 million
b) $10-100 million
c) $100-500 million
d) > $500 million

At what stage are the biotech companies you have invested in the current fund cycle? Please select all that apply.

a) Pre-seed / seed
b) Series A

c) Series B
d) Series C and beyond
e) Public

Have you invested in companies developing cell and gene therapies over the past 5 years (2018-2023)?

a) Yes
b) No (*respondents exit survey if no is selected*)

[If yes in the previous question] In which disease states are the companies you have invested in pursuing cell and gene therapies? Please select all that apply.

- Oncology/cancer
- Neurological disease
- Infectious disease
- Metabolic disease
- Hematology
- Endocrinology
- Pulmonary disease
- Ophthalmology
- Immunology
- Cardiovascular disease
- Others. Please specify:

[Exit question] What factors, if any, have influenced your decision not to invest in companies pursuing orphan drug indications?

Demographic Data (Innovators)

Within your role, are you responsible for strategizing the company's research and development pipeline or selecting its product portfolio?

a) Yes
b) No (*respondents exit survey if no is selected)*

What is your current role in biotech? Choose one option that is best fit.

a) Executive Leadership
b) Research and development
c) Clinical affairs
d) Reimbursement/Market access
e) Regulatory affairs
f) Commercial or strategic marketing
g) Sales or sales operations

What is the size of the organization you currently work in?

a) Large company (>10,000 employees)
b) Midsize company (500 to 10,000 employees)
c) Small company (50 to 500 employees)
d) Very small company (1 to 50 employees)

What is the primary source of funding for your biotech innovations?

a) Private equity or venture capital
b) Angel investor or family office
c) Publicly traded company
d) Grants
e) Others. Please specify:

Has your company developed cell and gene therapies over the past 5 years (2018-2023)?

a) Yes
b) No (*respondents exit survey if no is selected)*

[If yes in the previous question] In which disease states are the companies you have invested in pursuing cell and gene therapies? Please select all that apply.

- Oncology/cancer
- Neurological disease
- Infectious disease
- Metabolic disease
- Hematology
- Endocrinology
- Pulmonary disease
- Ophthalmology
- Immunology
- Cardiovascular disease
- Others. Please specify:

[Exit question] What factors have influenced your decision not to pursue orphan drug indications or develop cell or gene therapy recently?

Cell and Gene Therapy (Investors)

You indicated that you have invested in companies with cell or gene therapies. This section refers to the regulatory timeline of your products.

In your experience, what is the typical duration for your most advanced cell or gene therapy companies to progress from first FDA contact to receiving FDA approval?

a) Not yet started or still in the FDA approval process
b) 12 months or less
c) 1-5 years

d) 6-10 years
e) >10 years

Was this time more or less than the allocated timeline projected by the companies?

a) Substantially less
b) Less
c) Exactly the same
d) More
e) Substantially more

[If substantially less] What contributed to the quick turnaround time for your FDA approval process?

Choose the top three factors that drive the regulatory timeline.Reviewer or key staff turnover

- Lack of transparency of the approval process
- Inconsistent quality and participation of expert advisors
- Administrative delays
- Changing parameters for approval introducing during the review process
- Lack of proper preparation of the company in response to FDA requests
- Practical or financial challenges to address FDA requests
- Theoretical safety concerns unsupported by data
- Reasonable safety concerns supported by data
- Reviewer inexperience
- (Optional) Other issues:

Based on the issues mentioned previously, how will this impact your cell or gene therapy investments in the next 5 years?

a) Substantially decrease
b) Decrease
c) No change
d) Increase
e) Substantially increase

(Optional) Given the latest FDA investigation on the risk of T-cell malignancies for those who received Chimeric Antigen Receptor (CAR)-T therapy, what are your concerns on this issue and how do you think this would impact FDA approvals in the oncology space?

(Optional) What are the other regulatory challenges you're currently facing, if any?

Cell and Gene Therapy (Innovators)

You indicated that you have developed **cell or gene therapies**. This section refers to the regulatory timeline of your products.

In your experience, what is the typical duration for your most advanced cell or gene therapy companies to progress from first FDA contact to receiving FDA approval?

a) Not yet started or still in the FDA approval process
b) 12 months or less
c) 1-5 years
d) 6-10 years
e) > 10 years

Was this time more or less than the allocated timeline projected by your company?

a) Substantially less
b) Less
c) Exactly the same
d) More
e) Substantially more

Choose the top **three** factors that drive the regulatory timeline.

- Lack of transparency of the approval process
- Inconsistent quality and participation of expert advisors
- Administrative delays
- Changing parameters for approval introducing during the review process
- Lack of proper preparation of the company in response to FDA requests
- Practical or financial challenges to address FDA requests
- Theoretical safety concerns unsupported by data
- Reasonable safety concerns supported by data
- Reviewer inexperience
- (Optional) Other issues:

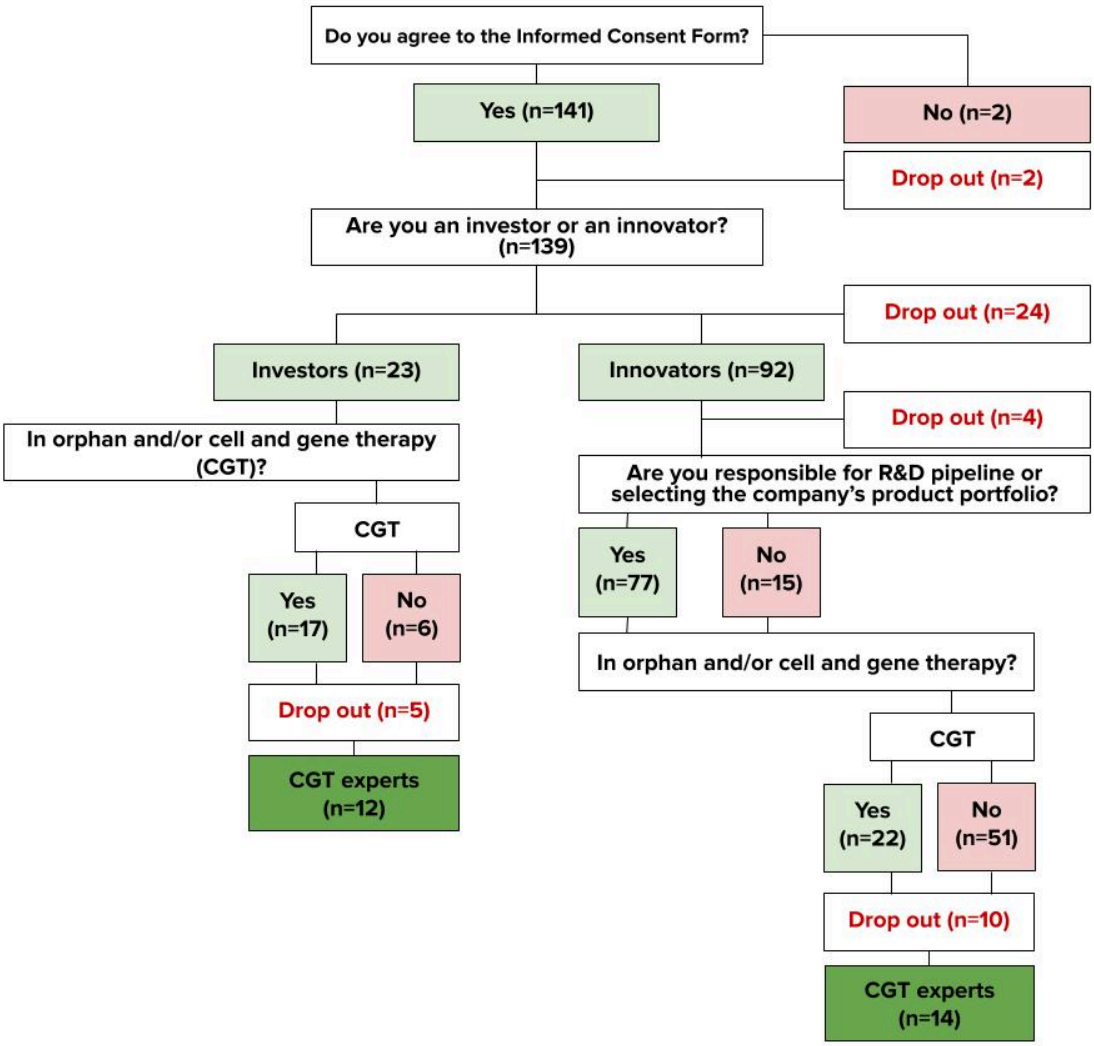
In your opinion, which disease states would be positively or negatively impacted based on the issues mentioned? You may choose to only answer for disease states you are knowledgeable about.
(From extremely negative, negative, neutral, positive, extremely positive)

- Oncology/cancer
- Neurological disease
- Infectious disease
- Metabolic disease
- Hematology
- Endocrinology
- Pulmonary disease
- Ophthalmology
- Immunology
- Cardiovascular disease
- Others. Please specify:

(Optional) What are the other regulatory challenges you're currently facing, if any?

We thank you for your time spent taking this survey. Your response has been recorded.

Appendix 2: Study Population



Appendix 3: Cell and Gene Therapy Investments per Disease States (n=16) (top) and R&D for Cell and Gene Therapy by Disease State(n=36)(bottom).