The Cost of Bringing a Biosimilar Product to Market—Expert Interviews

Generic Information Collection Request under OMB No. 0990-0421

Supporting Statement A

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Contact:

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A. JUSTIFICATION

The U.S. Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation (HHS/ASPE) has an ongoing interest in encouraging biosimilar product development to contain prescription drug costs and improve patient access. HHS/ASPE has awarded a contract to Eastern Research Group, Inc. (ERG) to (1) model the cost of development, including the costs of development of analytical methods, completing necessary clinical trials, and scaling up of manufacturing for a biosimilar product, by type; (2) examine factors that drive biosimilar market uptake; and (3) identify possible barriers to and incentives for bringing biosimilar products to market. In order to generate/validate several estimates that are inputs to the decision-making model of a biosimilar developer, we need to elicit opinions from key experts in the field, including academic researchers, industry representatives, intellectual property attorneys, pharmacy benefit managers, prescribing physicians, and clinical pharmacy managers, using semi-structured interviews to ask questions specific to each interviewee's area of expertise.

1. Circumstances Making the Collection of Information Necessary

The Biologics Price Competition and Innovation Act (BPCIA), enacted in 2009, created an abbreviated approval pathway for biosimilars—i.e., "generic" versions of brand name biologic drug products—much as the Hatch/Waxman legislation of 1984 facilitated quicker approval and market entry of generic versions of brand name chemical drugs. As of 2020, generic drugs comprise over 90 percent of prescription drugs dispensed in the U.S., but account for just 18 percent of prescription drug expenditures.[1] Biologic drug products are drug products derived from human, animal, or plant cells or tissues, rather than chemically synthesized. Biologics represent about 2 percent of prescriptions written in the U.S., but account for between 38 percent and 43 percent of annual drug expenditures in the U.S. Seven out of the 10 top selling drugs in the U.S. are biologics.

Although biosimilar development and market entry since BPCIA have been slow, the estimated savings generated by the relatively few biosimilar market entrants from 2015 to 2020 have been estimated at $35.8 billion. As of December 2022, FDA had approved 40 "original" biosimilar license applications (this number excludes supplemental applications for different doses or different delivery systems of the same medication) distributed across 11 biologic reference products. However, only 27 biosimilars, representing nine reference biologics, had been launched into their markets as of December 2022.

Biologics, relative to chemical drugs, are more complicated and costly to develop, get approved, and manufacture within requisite safety and quality standards. This accounts in part for their high cost. However, the drugs thus far developed have become instrumental in treating diseases such as rheumatoid arthritis, several types of cancer, auto-immune diseases, plaque psoriasis, diabetes, numerous inflammatory diseases, and many other serious conditions.

[1] Trish, E., Van Nuys, K., & Popovian, R., 2022. US Consumers Overpay for Generic Drugs.

However, the very high costs of most biologics have created accessibility issues for many patients and increased overall U.S. health care expenditures.

In order to develop policies that further facilitate biosimilar market entry, thereby creating competition within markets that will lower costs and increase patient access to life-saving medicines, ASPE requires a detailed model of biosimilar market entry decision making process that will allow projection of the expected net present value (eNPV) of a given biosimilar upon market entry.

2. Purpose and Use of the Information Collection

ASPE is seeking approval from OMB to conduct up to 40 virtual in-depth semi-structured interviews (IDSSIs) with individuals representing the following groups: manufacturers of biosimilars and biologic products; contract development and manufacturing organizations (CDMOs) of biosimilars; biosimilar and biologic trade groups; academic researchers with expertise in this subject area; attorneys experienced in patent challenges involving biosimilars and biologics; pharmacy benefit managers; and clinical pharmacy managers.

The information collected through this qualitative research, in conjunction with the quantitative analysis of biosimilar/biologic drug product sales and pricing data, will inform ASPE's research and programmatic efforts to incentivize biosimilar market entry, to enhance price competition within biologic drug markets where competition is limited or nonexistent, thereby expanding Americans' accessibility to life-saving or life-altering medications and slowing the growth of U.S. expenditures on biologic medications.

In order to reach this goal, the contractor, ERG, will aim to recruit representatives of biologic and biosimilar manufacturers and three to five people from each of seven other types of entities involved in development, market entry, and distribution of biosimilars, including: contract development & manufacturing organizations, wholesalers/ distributors, academic and other researchers, pharmacy managers, pharmacy benefit managers, intellectual property attorneys, prescribing physicians, and trade group representatives.

Recruitment of interviewees will be guided by the need to develop knowledge-based assessments of the costs associated with the numerous specific elements of biosimilar development, approval, licensing, manufacture, quality control, distribution, and sale of several categories of biosimilars. These categories include monoclonal antibodies, recombinant human hormone analogs, fusion proteins, tumor necrosis factor (TNF) inhibitors, and recombinant human granulocyte colony-stimulating factor analogs.

3. Use of Improved Information Technology and Burden Reduction

Interviews will be conducted via MS Teams, Zoom, or another video meeting platform convenient for the interviewee. Interviewees will be asked to allow audio recording of the

interview, which will avoid interviewee burden in the form of follow up calls or emails to fill in gaps in notes and also free interviewers from detailed note-taking, thereby avoiding distraction.

4. Duplication of Information

The contractor, ERG, has been performing an ongoing literature review and has found no models of the biosimilar market entry decision making process that account for the numerous variables for which we are seeking information. Some "models" make general assumptions about broad categories, such as assuming "lower development costs" or "regulatory impediments" and result in a broad range of potential costs for a non-specific biosimilar market entry.[2]

5. Reducing the Burden on Small Entities

Nine of the 10 companies that have launched biosimilars into the United States market since BPCIA was enacted in 2009 had revenue over $1.6 billion in 2022. The tenth company, Coherus, reported revenue of $211 million in 2022 and has 336 employees, well under SBA's limit of 1,250 to qualify as a small business in the "Pharmaceutical Preparation" sector. In addition to Coherus, ERG will seek interviews with personnel at several companies with biosimilars at various stages of development, and some of these may be small businesses. Because the burden is limited to three-quarters (0.75) of an hour for reading and responding to outreach emails followed by a one (1) hour virtual interview, there is no practicable way to reduce that burden any further for employees of small businesses.

Other small entities among our intended interviewees may include physicians, patent attorneys (some of whom may be at small firms), and academic researchers. The burden on these respondents will be the same as for representatives of large manufacturing firms, but the contractor hopes to offset their burden by providing a $150 honorarium in recognition of their willingness to be interviewed.

6. Consequences of Collecting the Information Less Frequently

This is a one-time data collection; these data have not previously been collected elsewhere.

7. Special Circumstances

There are no special circumstances. This request complies fully with regulation 5 CFR 1320.5 and will be voluntary and not generalizable.

[2] Brill, (2015). The Economic Viability of a U.S. Biosimilars Industry. Matrix Global Advisers. https://getmga.com/wp-content/uploads/2022/04/MGA_biosimilars_2015_web.pdf. Brill estimated development costs for a non-specific biosimilar at between $100 million and $300 million.

8. Consultations with Persons Outside the Agency

This data collection is being conducted using the Generic Information Collection mechanism through ASPE – OMB No. 0990-0421 therefore, no *Federal Register* notice is required.

9. Payment or Gift

ERG is prepared to offer some potential interviewees—those that will not be paid by their employers for the time taken up by the interview— a small honorarium of $150 in recognition of their willingness to take time away from their paid duties to participate in this collection.

10. Confidentiality

ASPE does not anticipate that the Privacy Act will apply to this data collection. The information sought during these interviews with industry personnel and others is not likely protected under any legal definition of confidentiality (e.g., confidential business information (CBI); doctor/patient and attorney/client confidentiality). However, ERG and ASPE have agreed contractually that that no interviewee or employer of an interviewee will be identified to ASPE or publicly identified as participating in these interviews, nor will any information enabling their identification be revealed by the ERG team. Likewise, people or companies refusing participation will not be identified.

ERG frequently assures this degree of privacy to participants in surveys and interview requests like this one to encourage unguarded responses and help blunt any concerns that information they provide might cause some enforcement action or other negative experience with a regulatory agency.

ERG is well-experienced in handling CBI and HIPAA-protected health care information. The project team will protect interviewees' privacy by maintaining all project files in password-protected folders on ERG's secure servers. Individual Excel and Word files containing interview data will be periodically de-identified.

11. Sensitive Nature

No questions will be asked that are of a personal or sensitive nature.

12. Burden of Information Collection and Costs to Respondents

This is a one-time data collection. The burden of the information collection and respondent costs for each type of responding entity are listed in the table below (see Table 1). The calculations assume a one-hour interview and an additional three-quarters of an hour for reading and responding to outreach emails.

The mean hourly wage rates are from the Bureau of Labor Statistics' May 2022 publication National Occupational Employment and Wage Estimates. The occupational categories associated with each wage rate appear in the table's footnotes.

Table 1. Estimated Annualized Burden Table and Annualized Cost to Respondents

Type of respondent	Number of Respondents	Number of Responses per Respondent	Average Burden Hours per Response [i]	Total Burden Hours	Mean Hourly Wage Rate	Total Respondent Cost
Manufacturer of Biosimilars	10	1	1.75	17.5	$51.95 [a]	$909.13
Manufacturer of Biologics	8	1	1.75	14	$51.95 [a]	$727.30
Contract Development & Manufacturing Organization	2	1	1.75	3.5	$51.95 [a]	$181.83
Wholesalers/ Distributors	3	1	1.75	5.25	$52.36 [b]	$274.89
Academic and other Researchers	3	1	1.75	5.25	$45.46 [c]	$238.67
Pharmacy Managers	2	1	1.75	3.5	$62.22 [d]	$217.77
Pharmacy Benefit Managers	2	1	1.75	3.5	$68.82 [e]	$240.87
Intellectual Property Attorneys	2	1	1.75	3.5	$78.74 [f]	$275.59
Health Systems	3	1	1.75	5.25	$121.15 [g]	$636.04
Prescribing Physicians	3	1	1.75	5.25	$121.15 [g]	$636.04
Trade Groups	2	1	1.75	3.5	$72.13 [h]	$252.46
Total	**40**	**NA**	**NA**	**70**	**NA**	**$4,590.59**

Source: U.S. Bureau of Labor Statistics. National Occupational Employment and Wage Estimates, United States https://www.bls.gov/oes/current/oes_nat.htm#19-0000.

[a] 17-2031 Bioengineers and Biomedical Engineers
[b] 1-3071 Transportation, Storage, and Distribution Managers
[c] 19-3099 Social Scientists and Related Workers, All Other
[d] 29-1051 Pharmacy Managers
[e] 11-3111 Compensation and Benefits Managers
[f] 23-1011 Lawyers
[g[29-1210 Physicians
[h] 11-2032 Public Relations Managers
[i] The figure is the sum of 0.75 hours for reading and responding to outreach emails and 1 hour of interview time.

13. Estimates of other Total Annual Cost Burden to Respondents or Recordkeepers/Capital Costs

There is no additional cost burden to respondents and no recordkeepers/capital costs.

14. Costs to Federal Government

The cost to prepare the information collection, conduct the interviews, and analyze and report the results of the study is $25,030.20 (see Table 2). This cost includes salaried labor for the

contractor's project team and other direct costs associated with planning and implementation of the interviews, and compilation and analysis of the results.

Table 2. Costs to Federal Government

Staff (FTE)	Average Hours per Collection	Average Hourly Rate [a]	Average Cost
Social Science Analyst, GS 11 [b]	140	$68.29	$9,560.60
Social Science Analyst, GS 15 [c]	70	$135.28	$9,469.60
Stipend to interviewees	40	$150.00	$6,000.00
Estimated Total Cost of Information Collection			**$25,030.20**

Source: US Office of Personnel Management (OPM). 2017. Salary Table 201-DCB (LEO) (Hourly Rate) - Effective January 2023. Available at https://www.opm.gov/policy-data-oversight/pay-leave/salaries-wages/salary-tables/23Tables/html/DCB_h.aspx (Accessed March 20, 2023).
[a] A 60 percent fringe and overhead factor is applied to the reported base wage of $42.68 for GS 11 Social Science Analyst and $84.55 for GS 15 Social Science Analyst.
[b] The allocated hours for the Social Science Analyst, GS-11 include drafting email correspondence to the target interviewees, responding to inquiries, notetaking during interviews, and drafting interview summaries.
[c] The allocated hours for the Social Science Analyst, GS-15 include conducting the interview and reviewing interview notes and summaries drafted.

15. Reason for Change

This is a new data collection.

16. Tabulation of Results, Schedule, Analysis Plans

Information collected under this generic clearance provides useful information, but it does not yield data that can be generalized to the overall population. Findings may be disseminated when appropriate, strictly following the HHS "Guidelines for Ensuring the Quality of Information Disseminated to the Public," and will include specific discussion of the limitation of the qualitative results discussed above. ASPE may also receive requests to release the information (e.g., congressional inquiry, Freedom of Information Act requests), and we will comply with those requests as appropriate.

17. Reason(s) Display of OMB Expiration Date is Inappropriate

We are requesting no exemption.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

These activities comply with the requirements in 5 CFR 1320.9.

LIST OF ATTACHMENTS

Attachment A – Invitation/Outreach Email
Attachment B – Interview Guide

ATTACHMENT A

INVITATION/OUTREACH EMAIL

Dear____,

My name is [name] and I am a [job title] at Eastern Research Group, Inc. (ERG). We have been contracted by US Department of Health and Human Services Office of the Assistant Secretary for Planning and Evaluation (HHS/ASPE) to conduct an exploratory study to investigate 1) the cost of development, testing, approval, manufacture, and commercialization of biosimilar products, 2) perceived barriers to market entry by biosimilar companies, and 3) potential incentives to encourage entry and improve market uptake of biosimilar products. As part of that study, we are reaching out to experts on the biosimilar industry to elicit their opinions on these topics.

We are contacting you because we would like to interview you given your expertise in the [applicable biosimilar topics]. If you are interested in participating, we'd ask that you please reply with at least two (2) preferred 1-hour time windows between [date] and [date] that would work for an interview to be conducted via Teams/Zoom.

Please note that we consider these interviews to be PRIVATE; ERG will not identify any interviewees—or their companies—in any of our work products, nor associate specific responses with individuals. Only the members of ERG's project team will have access to such information.

Thank you for your time and consideration. I look forward to hearing from you soon. If you have any questions about participation, please do not hesitate to reach out.

Sincerely,
[name]

ATTACHMENT B

INTERVIEW GUIDE

Information Collection on the Biosimilar Industry

The questionnaire will be administered by an experienced interviewer via the web (Teams/Zoom) or telephone.

Interviewer Script

Thank you for taking the time to talk with us today. I am [name] and this is [name(s)], from Eastern Research Group, Inc. (ERG). It's a pleasure to meet you [or talk with you again].

As noted in our email to you, we are working on a project for the US Department of Health and Human Services Office of the Assistant Secretary for Planning and Evaluation (HHS/ASPE) to conduct an exploratory study to investigate 1) the cost of development, testing, approval, manufacture, and commercialization of biosimilar products, 2) perceived barriers to market entry by biosimilar companies, and 3) potential incentives to encourage entry and improve market uptake of biosimilar products.

As part of that study, we are reaching out to experts on the biosimilar industry to elicit their opinions on these topics. The purpose of this interview is to ask you questions about [applicable biosimilar topics]. This interview should take about an hour. I will ask questions, and [name(s)] will take notes. ERG will keep your identifying information private. We will share only anonymized results outside our internal project team.

Here are standard government statements about the voluntary and confidential nature of this information collection:

Public reporting burden for this collection of information is estimated to average 60 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other suggestions for reducing this burden to Susan Jenkins. Notwithstanding any other provisions of the law, no person is required to respond to, nor shall any person be subjected to a penalty for failure to comply with, a collection of information subject to the requirements of the Paperwork Reduction Act, unless that collection of information displays a currently valid OMB Control Number. The OMB Control Number for this information collection is OMB Control Number 0990-0421.

Your participation in this study is completely voluntary. In instances where respondent identity is needed (e.g., for follow-up), this information collection fully complies with all aspects of the Privacy Act and data will be kept private by ERG to the fullest extent allowed by law. ERG will

not identify any interviewee, or provide any information that would enable their identification, in any report or publication.

Do you voluntarily agree to be interviewed for this study?

Do you permit us to record this interview (please note that the recording will only be available to the ERG team members)?

Do you have any questions before we start?

After any questions have been addressed, proceed to conducting the interview.

DATE:_____
ERG INTERVIEWER(S):_____
INTERVIEWEE(S):_____

GENERAL QUESTIONS

1. Can you briefly tell us about your background on biosimilars? [INTERVIEWER: Inquire about current job position and responsibilities.]

2. Can you tell us what you consider to be the current major trends in the U.S. biosimilars market and among biosimilar manufacturers? [INTERVIEWER: Consider following up with]:

2.1. What have been the major barriers to biosimilar market entry since BPCIA was enacted?

2.2. Are there any general market entry decision-making principles that most companies consider, independent of any differences in biosimilar types?

2.3. What factors impact the number of biosimilar competitors that will enter a market?

2.4. What is the long-term trend for markets with biosimilar competition? Are these markets shrinking in terms of volume? Will the reference product and biosimilar eventually reach a price equilibrium, or will the reference product ultimately leave the market due to decreasing revenues?

2.5. Will biosimilar competition prompt reference product companies to develop next-line products?

3. What are the important differences between markets with biosimilars? How do these differences impact adoption, market share, entry decisions? [INTERVIEWER: Depending on the background of the interviewee, consider following up with]:

3.1. Compared to other biosimilars, infliximab (biosimilars: Inflectra, Renflexis, Avsola; reference product: Remicade) had slower initial adoption in terms of market share. Then in 2021, its market share began to increase more rapidly, similar to other biosimilars. What factors could have contributed to initial adoption being slower?

3.2. For epoetin alfa (biosimilar: Retacrit; reference product: Epogen), biosimilar market share was increasing consistently, but then had a sharp drop in 2022. This trend has not occurred in other US biosimilar markets. Why might this have happened for epoetin alfa? What distinguishes the epoetin alfa market from the other biosimilars markets?

3.3. What factors distinguish insulin glargine from the other biosimilars markets? In the US and abroad, why is insulin glargine still so dominated by the reference products despite biosimilar/interchangeable competition?

3.4. Aside from Humira, what biologics markets/products are likely to see new biosimilar competition? What makes these good candidates for biosimilar entry?

3.5. What chemical drugs could see competition from biosimilars in the future? What makes these good candidates for biosimilar entry?

4. What are biosimilar manufacturers' major concerns regarding actions of reference product manufacturers? (e.g., patent walls, the patent dance, protracted IP litigation and costs, rebates, formulary position, CMS and private insurer reimbursement policies, potential FTC allegations of anti-competitive IP settlements, etc.)

5. [FOLLOW-UP: To what extent does the potential for such actions by reference product manufacturers inhibit biosimilar development?]

6. What are the impacts of practitioner attitudes or physician education on biosimilar adoption?

MANUFACTURER'S DECISION TO ENTER A BIOSIMILAR MARKET

7. In your experience, do most biosimilars manufacturers have an ongoing, organized process to evaluate potential markets and to decide which biosimilar markets to enter and which to avoid?

8. What are the major barriers and inducements to entering a biosimilar market? For instance:

8.1. Does the market for a reference product have to be above a certain dollar amount?

8.2. Does the market for a reference product have to be above a certain number of prescriptions per year?

8.3. Is the required size of a prospective market lower if there are no biosimilar competitors already in the market? Does the required size of the market rise as the number of biosimilars already in the market increases?

8.4. How do companies define small, medium, and large biosimilar markets?

8.5. How does the expected number of biosimilar entrants impact your decision about whether and when to enter a market? Is being the first biosimilar entrant an important consideration for you?

9. What would you say are the [other] major barriers for companies considering entry into a biosimilar market? [INTERVIEWER: Ask about the following factors, at least]

9.1. Reference product is in patent or out of patent.

9.2. Anticipated difficulty of obtaining enough of reference product for biosimilar development, comparative testing, and clinical trials.

9.3. Number and identity of current or anticipated competitors in the market.

9.4. Potential impact of a clinical trial setback or litigation setback on company's market value or share price.

9.5. Time required for in vitro, in vivo, and clinical studies.

9.6. Time required for CDER approval.

9.7. Difficulty in establishing a distribution network or supply chain for a new biosimilar.

9.8. Difficulty of setting up or contracting for production.

9.9. (Are any biosimilar manufacturers contracting their development or manufacturing?)

9.10. Reference product manufacturer bundling reference product in a contract with other drugs to thwart biosimilar uptake by customers even if biosimilar costs less.

9.11. Other factors?

10. At what stage of biosimilar development do most companies, in your experience, begin to engage with CDER?

11. Do most companies have a distribution network already set up before deciding to enter a biosimilar market? Do some companies have difficulty in placing a new biosimilar product with wholesalers or distributors? For what reasons?

12. If the biosimilar's BLA is approved, what is the probability of the sponsor successfully launching the product? Why would a company NOT go into production after CDER approval? (e.g., IP litigation, settlement agreement, other reasons)

13. How long does it take a typical biosimilar to hit peak-year sales?

MANUFACTURER'S COSTS TO ENTER BIOSIMILAR MARKETS

14. What are the approximate cost ranges—and/or the relative proportion of total costs—for the following elements of bringing a biosimilar to market?

14.1. Analysis of reference product.

14.2. Initial biosimilar development for analysis

14.3. Shelf-life studies.

14.4. Obtaining adequate supply of reference product

14.5. Cost of APIs, excipients.

14.6. Cost of manufacturing trial quantities of biosimilar.

14.7. Cost of designing manufacturing process, setting up quality monitoring

14.8. CDER approval process.

14.9. Patent litigation.

14.10. Establishing a distribution network.

14.11. Costs of commercialization, i.e., pre-launch and post-launch marketing.

14.12. Establishing a supply chain for a new biosimilar.

15. What is the approximate overall success rate for biosimilars, i.e., what is the probability of a biosimilar in development advancing through development, BLA approval, and manufacture to product launch?

16. Are there differences in the relative costs to develop and obtain approval for the different types of biosimilars, such as monoclonal antibodies, enzymes, recombinant glycoproteins, insulins, tropic hormones, interferons, or others?

17. How long do safety and efficacy clinical trials for biosimilars usually cost and how long do they take on average? Are clinical trials mainly conducted in the U.S., Europe, India, or…?

THOUGHTS ON POTENTIAL INCENTIVES

18. In your opinion, what types of government or agency policies would help stimulate more investment in biosimilar development? [FOLLOW-UP: Specifically ask if the 12-month exclusivity period for interchangeables has been an effective incentive for market entry.)

INTERVIEW WRAP UP

19. Is there anything else that you would like to point out that we have not asked about?

20. Is it okay for us to contact you if we have any follow-up questions?

21. Would you like to recommend others that you think we should speak to?

Thank you for your time.