FDA Answers Your Questions About the STAR Pilot Program

February 15, 2024, 1:00 PM (ET)

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Overview of FDA Split Real Time Application Review (STAR) Pilot Program

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FDA Answers your Questions about the STAR Pilot Program – February 15, 2024
Learning Objectives

• Discuss the background of STAR pilot program
• Describe the STAR pilot program
• Outline CDER’s review of STAR pilot program applications
• Discuss the STAR pilot program website
• Discuss STAR pilot program assessment
• List resources for Industry
Background

Prescription Drug User Fee Act (PDUFA):

• STAR introduced as a new pilot program under PDUFA VII
• Available to applicants beginning in FY 2023 (October 1, 2022)

Website: https://www.fda.gov/media/151712/download
Why the new STAR pilot program?

During user fee negotiations, Industry signaled that generally, data sets and other application contents are ready in advance of the Clinical Study Report (CSR), Integrated Summary of Safety (ISS), and Integrated Summary of Effectiveness (ISE).

Waiting for the CSR, ISS, and ISE can delay NDA/BLA submission to FDA.

Allowing submission of all other parts of a supplemental marketing application to start FDA review in advance of CSR, ISS, and ISE availability may enable earlier access to treatment addressing an unmet medical need.
Goal of the STAR pilot program

To shorten the time from the date of complete supplement submission to the action date to allow earlier patient access to therapies that address an unmet medical need.
What is the STAR pilot program?

• A pilot program for qualified priority efficacy supplements

• Submitted in two parts to enable an earlier review and action
STAR Pilot Program Overview

STAR Program Shifts Review But Not PDUFA Clock

STAR Review

PDUFA Priority Review Clock (6 months)

STAR Entry Request

Sponsor Meeting

Part 1 Submission

Begin Application Review

Part 2 Submission*

Filing Meeting

Filing Letter

STAR Target Action Date

At least 1 mo. before PDUFA Goal Date

PDUFA Goal Date

*The Part 2 Submission is usually received ~2 months after Part 1, but no more than 3 months after Part 1.
STAR Pilot Program Entry Request: Format

**Option 1:** Request as stand-alone T-con (no discussion of supplement content/format)

or

**Option 2:** Request as Part of a Type B pre-sNDA/sBLA meeting (to also discuss supplement content/format)
STAR Pilot Program Entry Request: Content

- Topline results from adequate and well-controlled clinical trials
- Proposed labeling
- Explanation of how the supplemental application meets STAR pilot program criteria
STAR Pilot Program Eligibility Criteria

1. Clinical evidence from adequate and well-controlled investigation(s) indicates that the drug may demonstrate substantial improvement on a clinically relevant endpoint(s) over available therapies.

2. Application is for a drug intended to treat a serious condition with an unmet medical need.
STAR Pilot Program Eligibility Criteria (continued)

3. No aspect of the submission is likely to require a longer review time

4. No chemistry, manufacturing, or control (CMC) information that would require a foreign manufacturing site inspection
STAR Pilot Program Split Submission: Part 1

Contains **all** elements of the supplemental application *except*:

- Clinical study report (CSR)
- Integrated summary of effectiveness (ISE)
- Integrated summary of safety (ISS)
STAR Pilot Program Split Submission: Part 1 (continued)

Part 1 submission should also include:

- Tables, Figures, and Listings
- Protocol and amendment(s) for pivotal trial(s)
- Statistical analysis plan and statistical analysis program for pivotal trial(s)
- Sponsor’s high-level assessment summary of the safety and efficacy results
- Death summaries
STAR Pilot Program Split Submission: Part 1 (continued)

• If FDA identifies substantive **missing information**, reviews will stop

• A *Revocation of STAR Status* letter may be issued
STAR Pilot Program Split Submission: Part 2

- **Contains:** CSR, ISE, ISS

- **Timeline:**
  - PDUFA clock starts with Part 2 submission
  - Must be received by FDA no later than 3 months after Part 1 submission
STAR Pilot Program Split Submission: Part 2 (continued)

• If FDA identifies substantive **missing information**, reviews will stop

• A *Revocation of STAR Status* letter may be issued

• A *Refuse to File (RTF)* letter may be issued
STAR Pilot Program
Review Timeline Summary

• Review begins with the receipt of Part 1 submission
• PDUFA clock starts with receipt of Part 2 submission
• FDA will generally target an “expedited review”, meaning an action at least 1 month before the PDUFA goal date
STAR Pilot Program Resources

Split Real Time Application Review (STAR)

Under the Prescription Drug User Fee Act (PDUFA) VII Commitment Letter\(^4\), FDA is creating the Split Real Time Application Review (STAR) pilot program.

**Overview**

FDA is establishing a STAR pilot program, which aims to shorten the time from the date of complete submission to the action date, in order to allow earlier patient access to therapies that address unmet medical need. The STAR pilot program will apply to efficacy supplements across all therapeutic areas and review disciplines that meet specific criteria. Accepted STAR applications will be submitted in a “split” fashion, specifically in two parts with the components submitted approximately two months apart.

FDA will begin to review the data once the agency receives the complete Part 1 Submission. The PDUFA review clock will start once the agency receives the Part 2 Submission, which will include the final clinical study report(s), the Integrated Summary of Safety, and Integrated Summary of Effectiveness. The program applies to both drugs and biologics, collectively referred to as drug(s). STAR is available for certain supplemental new drug applications (sNDAs) and supplemental biologics license applications (sBLAs) that propose new uses of approved therapies to address an unmet medical need. The program is available across all therapeutic areas.

**STAR Eligibility Criteria**

[https://www.fda.gov/drugs/development-resources/split-real-time-application-review-star](https://www.fda.gov/drugs/development-resources/split-real-time-application-review-star)
STAR Pilot Program Assessment

- FDA will conduct an interim assessment by the end of FY 2025
- FDA will also conduct a public workshop by the end of Q2 in FY 2026
- Outputs from the assessment and workshop will be published in a publicly available report
Frequently Asked Questions

**Question 1:** When does FDA begin their review of a STAR application?
Frequently Asked Questions

**Question 1:** When does FDA begin their review of a STAR application?

**Response to Question 1:**
Upon receipt of the STAR Part 1 submission
Frequently Asked Questions

**Question 2:** When does the PDUFA clock start for a STAR application?
Question 2: When does the PDUFA clock start for a STAR application?

Response to Question 2: Upon receipt of the STAR Part 2 submission.
Question 3: When is the Integrated Summary of Safety submitted?
Question 3: When is the Integrated Summary of Safety submitted?

Response to Question 3:
With the Part 2 Submission
Frequently Asked Questions

**Question 4:** What is the difference between STAR and the Real Time Oncology Review (RTOR)?
Frequently Asked Questions

**Question 4:** What is the difference between STAR and the Real Time Oncology Review (RTOR)?

**Response to Question 4:**

STAR is a PDUFA program open to development programs from any therapeutic area. RTOR is not a PDUFA program and is only available for oncology drug products.
Question 5: Does the STAR pilot program apply to oncology products, or should the sponsors of those products apply only to RTOR?
Frequently Asked Questions

**Question 5:** Does the STAR pilot program apply to oncology products, or should the sponsors of those products apply only to RTOR?

**Response to Question 5:**

Both STAR and RTOR are available to oncology products. However, sponsors should discuss their preference with the RPM of the relevant oncology division, for their particular product, to receive further guidance.
Question 6: What happens if an applicant does not submit the Part 2 submission within 3 months of the Part 1 submission?
Question 6: What happens if an applicant does not submit the Part 2 submission within 3 months of the Part 1 submission?

Response to Question 6:

If Part 2 is not submitted within 3 months of Part 1, the application will be removed from the STAR pilot program.
Frequently Asked Questions

**Question 7:** How does STAR relate to Breakthrough Therapy Designation (BTD)?
Question 7: How does STAR relate to Breakthrough Therapy Designation (BTD)?

Response to Question 7:

Both programs utilize the same criteria for clinical evidence. A formal BTD granted is not required for STAR entry.

BTD primarily provides benefits during the drug development or IND.

STAR is intended to provide benefit during the review of the supplemental marketing application.
Frequently Asked Questions

**Question 8:** Is STAR only applicable for supplementary NDAs or BLAs?
Question 8: Is STAR only applicable for supplementary NDAs or BLAs?

Response to Question 8:
Yes, currently STAR is only available for efficacy supplements which meet the STAR criteria.
Frequently Asked Questions

Question 9: If a drug development program and packaging take place in the United States (US), but active pharmaceutical ingredient (API) is manufactured outside of the US, would this disqualify from participating in the STAR pilot program?
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Response to Question 9:

Supplemental applications that require an inspection of a foreign manufacturing site do not qualify for STAR.
Resources

1. PDUFA VII Commitment Letter
2. FDA STAR Website
Summary

• The goal of the STAR pilot program is to shorten “the time from the date of complete submission to the action date, in order to allow earlier patient access to therapies that address an unmet medical need”

• A STAR application is submitted in two parts to enable FDA to start their review earlier and potentially take an earlier action

• The STAR pilot program is limited to Priority Efficacy Supplements that meet certain criteria
STAR Pilot Program Overview

STAR Program Shifts Review But Not PDUFA Clock

STAR Review

PDUFA Priority Review Clock (6 months)

STAR Entry Request  Sponsor Meeting  Part 1 Submission  Begin Application Review  Part 2 Submission*  Filing Meeting  Filing Letter  STAR Target Action Date  PDUFA Goal Date

At least 1 mo. before PDUFA Goal Date

*The Part 2 Submission is usually received ~2 months after Part 1, but no more than 3 months after Part 1.
Questions?

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Closing Thought

Remember to include all components required for the Part 1 and Part 2 submissions in order to utilize the benefits of the STAR pilot program.