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FDA CBER OTP Town Hall:
Best Practices for Preparing BLA Submissions for Cell and Gene Therapy Products

June 4, 2026

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RAMANI SISTA, PhD: Good morning, everyone, and thanks for joining us for today's virtual town hall. Today's event is hosted by the Office of Therapeutic Products, or OTP for short, which is part of the Center for Biologics Evaluation and Research here at the FDA. I am Ramani Sista, and I'm the director for the Office of Review Management and Regulatory Review in OTP. I'm so excited that you could join us today at OTP's 11th town hall, "Best Practices for Preparing BLA Submissions for Cell and Gene Therapy Products." Next slide, please.

We know that BLA submission is top of mind for many of our sponsors, especially as more cell and gene therapies make their way from clinical trials to market. And it's great to have so many first-time BLA submitters joining us today. We know the submission and review process can be a lot to navigate, so we are going to dive into some of the common challenges our sponsors face and, more importantly, how to overcome them.

We'll also cover pre-BLA and milestone meetings, including how to request a pre-BLA meeting with OTP and how to get the most out of that conversation; submission package preparation, with practical tips for organizing your BLA so it's complete and ready for review; and navigating the application process, including tools and resources to help you understand the review timelines, filing procedures, what to expect from regulatory actions, and more.

Our goal today is to provide practical, actionable information to help our sponsors approach the BLA process with clarity and confidence. Whether you are early in your planning or actively preparing a submission, we hope today's conversation will be a valuable resource, and you will walk away with some practical insights. Next slide, please.

Before we begin, I'd like to share some background about OTP's virtual town hall series for anyone who's new to it. OTP launched our virtual town hall series in 2022 to stay connected with product developers and researchers. These town halls have a Q&A format, and our goal is to answer your questions to help support development of OTP-regulated products. We've hosted town halls on a variety of topics, including cell and gene therapy CMC, facility readiness for BLAs and post-licensure changes, and tips for regulatory interactions with OTP. You can revisit the recordings and transcripts from our previous town halls on FDA.gov. We always welcome your feedback and topic suggestions. Your input helps make these events as useful as possible for our sponsors and stakeholders, so please keep that feedback coming. Next slide, please.

There are a few housekeeping items I'd like to share before we get started. Today's town hall is being recorded, and the recording will be posted on FDA's website in the coming days and on the FDA YouTube channel. Closed captioning for this event is available directly on YouTube.

We received a lot of great questions in advance and look forward to working through those with you today. In the latter portion of today's event, we'll switch to live questions. We encourage everyone tuning in today to share their questions. To submit a question for our panelists during today's event, please email the questions to OTPevents@fda.hhs.gov. The email is listed here on the screen and also in the YouTube description to make it easy for you to copy and paste. So please go ahead and start sending us your questions now, and we'll do our best to address as many as we can. But please note, we are not able to answer any questions about specific products, draft guidance documents, or guidance documents that are currently under development.

One quick note before we dive in: we are keeping the focus of today's town hall on the BLA submission process, so we won't be getting into discipline-specific questions like those related to CMC or clinical topics. We know those are important topics, and we hope to cover them in a future town hall, so please keep those questions handy for next time. I also encourage you to take a look at some of our previous town hall recordings, which may address some of those questions. Next slide, please.

I'd like to take a moment to introduce our fantastic team of experts for today's virtual town hall. Starting with our moderator, Shalini Seetharaman. Shalini is a Lead Regulatory Project Manager in ORMRR, and she's joined by our panelists: Jessica Boehmer, ORMRR's Associate Director for Regulatory Policy; Tyree Newman, Chief of Branch 3; and Nadia Whitt, Chief of Branch 1. A big thank you to our moderator and panelists for their time and for sharing their expertise today. Next slide, please.

And with that, I will now hand things over to Shalini. Thank you all again for joining us today. Shalini, it's all yours.

SHALINI SEETHARAMAN, MS: Thanks for the great introduction, Ramani, and welcome, everyone. As Ramani mentioned, my name is Shalini Seetharaman. I will be the moderator for today's town hall.

As far as the agenda goes, first we will start with questions that were submitted ahead of time and then move on to questions coming in live through our email inbox. Please keep those

questions coming. Again, the email address is here on the screen, and it is OTPevents@fda.hhs.gov.

We will try to answer as many questions as we can, but as we mentioned, we will not be able to answer any questions about specific products or guidance documents that are currently under development and not published. And just a reminder that this town hall is being recorded, and you can revisit the full discussion at a later time after it's posted on our website. All right, let's get to it. Next slide, please.

Okay, starting off with an overarching question that we often hear from sponsors, and a great way to kick off today's Q&A. This question is for Nadia.

We are a small biotech company, and this is our first time submitting a BLA for a rare disease. We've been working on this biologic product for years, and we are finally ready to submit, but honestly the whole process feels overwhelming. Can you walk us through what we should expect during the review process, and is there anything we should make sure we have in order before we hit submit? Nadia, over to you.

NADIA WHITT, MS: Absolutely. Thanks, Shalini, and I'm glad we're starting here because this comes up a lot. The most important thing you can do before you submit is request a pre-BLA meeting with CBER. It's specifically designed to help sponsors identify gaps before filing, and it can save a significant amount of time down the road.

In terms of where first-time submitters most commonly run into trouble, CMC is probably the biggest one. We see submissions where the manufacturing process description is incomplete, specifications aren't adequately justified, or stability data doesn't cover the proposed shelf life. It's worth investing real time there before you submit.

On the clinical side, make sure your integrated summaries of safety and efficacy are thorough and clearly tied to your labeling claims. We often see a disconnect between what the data shows and what the sponsor is proposing in the label, and that's something we'll need to work through during review.

For nonclinical, ensure your studies are GLP-compliant where required and that study reports are complete. Missing raw data or incomplete reports are more common than you'd think.

And don't underestimate information in Module 1. Missing forms, incomplete financial disclosures, and labeling formatting issues are surprisingly common and can slow things down significantly.

FDA has resources and programs tailored to exactly your situation, and we want to see you succeed. So, make sure you reach out early and often. That's the best advice I can give. Back to you, Shalini.

SEETHARAMAN: Great answer. Thanks so much, Nadia. That was really helpful, and I think it's a good reminder for all our sponsors. And moving on, building on what Nadia mentioned about scheduling a pre-BLA meeting in her response, I would like to spend a few minutes diving into more specifics about what a pre-BLA meeting is and how to get the most out of it. So, the next question is for Tyree.

Tyree, is a pre-BLA meeting required before submitting a BLA?

TYREE NEWMAN, MDiv: Thank you for the question. I would like to begin by first stating that we highly recommend you take advantage of the opportunity to have the pre-BLA meeting with the review team, understanding that there is no disadvantage to having the meeting, including other early meeting interactions, sort of like an end-of-phase meeting. Again, the pre-BLA meeting is your best opportunity to ensure that we know exactly what to expect in your application, as well as for the FDA to inform you of what we expect to see at the time of BLA submission. Now, with that said, a pre-BLA meeting is not required prior to the BLA submission, but as stated earlier, highly recommended. Thank you.

SEETHARAMAN: Thanks, Tyree. Okay, we'll continue on with our theme of pre-BLA meetings. Our next question is for Jessica.

Jessica, when should a pre-BLA meeting be requested in relation to the planned BLA submission date?

JESSICA BOEHMER, MBA: Thank you, Shalini. In general, you should plan to submit your pre-BLA request no later than four months prior to the anticipated BLA submission date. The pre-BLA meeting, if granted, will usually be scheduled to occur within 60 days of our receipt of the meeting request. Remember that OTP will only grant one pre-BLA meeting for a specific product and indication, and generally we will not grant separate clinical or CMC-focused pre-BLA meetings. Back to you, Shalini.

SEETHARAMAN: Thanks so much, Jessica. So our next two questions are all about preparing for your pre-BLA meeting. This question is for Nadia.

Nadia, are there common errors sponsors make when preparing for pre-BLA meetings? And what is recommended by OTP?

WHITT: Yes, there are some common errors, and we see a few patterns come up consistently enough that they're worth calling out directly.

First, some sponsors skip the pre-BLA meeting altogether. And as you heard, we recommend that you should have that meeting; you're missing a real opportunity to discuss critical components with FDA before you file. We also see sponsors submit meeting requests too late, sometimes after one or two modules of their BLA have already been submitted. That leaves insufficient time for meaningful discussion before the full BLA submission comes in.

Meeting packages are another common challenge. Some are too dense, making it difficult for OTP to prepare their preliminary responses, while others can be too sparse to support substantive discussion. There's a balance, and it matters.

We also see sponsors occasionally use the meeting itself to raise new questions or proposals that weren't in the original package. This puts OTP in the position of not being able to respond meaningfully in the moment.

And finally, sponsors sometimes spend too much time of the meeting on presentations rather than on clarifying dialogue, which makes these meetings most valuable.

The common thread across all of these is preparation. The sponsors who get the most out of pre-BLA meetings are those who prepare early, focus their questions sharply, and come ready to have a real conversation. Back to you, Shalini.

SEETHARAMAN: Thanks, Nadia. So, one more question about pre-BLA meetings.

Tyree, what are your recommendations to structure our time to make the most of the 60 minutes during a pre-BLA meeting? Should there be detailed presentations, or should we head straight to the discussion of meeting question responses?

NEWMAN: Thank you, Shalini. I'll probably reiterate some of the things that Nadia has already said.

Beginning first: understand this is your meeting, and to make the best use of everyone's time, which means being able to address all of your questions, we recommend that if you desire to

open with an introduction, it be brief. Let me reiterate that — make sure that it's brief, meaning the introduction should be no more than a few minutes.

Then we recommend you prioritize the questions you wish to discuss in the order of importance, as well as addressing any areas where you found our preliminary responses to be unclear.

With that in mind, we also prefer that you reserve possibly the last 5 to 10 minutes or so for your team to summarize the key discussion points, any agreements or disagreements, and action items, to confirm we are all on the same page.

It has been our experience that sponsors who use their time this way consistently get more out of the meeting than those who spend a significant amount of time on presenting. And to reiterate, the time allocated for the closing summary is extremely valuable because it gives both parties a shared understanding of the discussion before the official meeting summary from the agency is issued, which is typically within 30 days.

Lastly, please understand that this discussion and decisions are typically based on the questions and information provided in the meeting package. Therefore, any new questions that are posed at the time of the meeting and were not a part of the initial briefing package may be unable to be addressed by the review team. Hopefully this was helpful. Back to you, Shalini.

SEETHARAMAN: Well said, Tyree. Thank you. So we are going to focus on our next few questions about rolling reviews. But before we go to our next question, I just want to share a reminder that if you have any questions for our panelists for today's town hall, please submit those to our email inbox. You can see it here on the screen: OTPevents@fda.hhs.gov. So, for the first question about rolling reviews, it is for Jessica.

When is it appropriate to request a rolling review for a BLA?

BOEHMER: Thank you, Shalini. First, I should note, as a reminder, rolling review can only be granted for applications that were granted RMAT, breakthrough therapy, or fast-track designation. And you should discuss your plan for rolling review at the pre-BLA meeting.

I know we said a pre-BLA meeting is not necessarily required, but this is where there's an exception. If there is preliminary agreement regarding your plan for rolling review at the pre-BLA meeting, you may then proceed with the official submission of the rolling review request to the associated IND.

The review team will review the proposal and will determine if the request is granted or denied. You should not start submitting modules to your BLA until you receive the rolling review request granted letter from your RPM. Back to you, Shalini.

SEETHARAMAN: Thanks, Jessica. Another question about rolling reviews. This one is for Nadia.

When is the BLA considered received if under rolling review?

WHITT: Thanks, Shalini. That's a great question for those that are pursuing rolling review. The rolling review is not considered received until the final submission. This is when you've submitted the final module, and that's the date that starts the review clock. At this point, you'll receive an acknowledgement letter confirming receipt.

Just keep in mind that acknowledgement letters are only issued following the final module, so don't be concerned if you don't receive one after earlier submissions. Back to you, Shalini.

SEETHARAMAN: Thanks, Nadia. Okay, let's move on to our next question, and this one is for Tyree.

Tyree, when should a sponsor request a priority review designation?

NEWMAN: Thanks, Shalini. We recommend an applicant should first consider discussing the priority review designation at the time of the pre-BLA meeting. Then, after receiving feedback, if you still desire priority review designation, make sure you also request it in your marketing application. Priority review designation will then be considered during the initial review, and the applicant will then be notified if it is granted at the time of the filing communication. Thank you, Shalini.

SEETHARAMAN: Thanks, Tyree. Okay, Jessica, let's circle back to you with the next question. This question is from the sponsor:

Does your planned application qualify for the Real-Time Oncology Review process or Project Orbis? What about the Assessment Aid?

BOEHMER: Thank you, Shalini. Currently, applications submitted to CBER's Office of Therapeutic Products, or OTP, are not eligible for the RTOR program or for review under Project Orbis. These programs are specific to applications reviewed in CDER in conjunction with the Oncology Center of Excellence.

However, the Assessment Aid, on the other hand, is a tool that OTP has adopted from OCE, and we encourage use of the Assessment Aid in submission with your BLA. We highly recommend discussing your proposed plan to use the Assessment Aid at your pre-BLA meeting with FDA. Back to you, Shalini.

SEETHARAMAN: Great answer. Thanks, Jessica. Let's shift gears a bit and talk more about preparing your BLA submission. The first question here is for Nadia, and the sponsor asked:

When preparing a BLA submission, can CMC information be incorporated into the BLA by reference to a master file? Nadia.

WHITT: Thanks, Shalini. For questions about master files, the FDA's draft guidance on drug master files from October 2019 is probably one of the best resources available. That guidance specifically addresses FDA's approach to the use of the master file in BLA applications under the Public Health Service Act, including BLAs from cell and gene therapies.

The key takeaway is that FDA generally does not permit applicants to incorporate drug substance or drug product manufacturing information by reference to a master file. At the BLA stage, we expect all manufacturing information to be submitted directly in the BLA, because a BLA holder is generally expected to have knowledge of and control over the manufacturing process for the biological product for which it is seeking licensure. Back to you.

SEETHARAMAN: Thanks, Nadia. That was really helpful, as this question comes up a lot. And before we move on, I do want to encourage folks to please keep those live questions coming via our email inbox, and remind everyone that we aren't able to address any CMC or clinical-focused topics today, but to keep those questions handy for a future town hall.

Okay, moving on to our next question. This one is for Tyree, and it's about the actual BLA submission process, specifically about the electronic common technical document, which we commonly refer to as eCTD.

In preparing for our BLA submission, we've been connecting with other sponsors who have not been through this process, and we learned that one of them received a technical rejection notice on their submission, which was a bit of an eye-opener for us. We want to make sure we do not go down the same road. Can you walk us through the most common reasons a BLA submission gets technically rejected, and what we should be doing now to prevent that from happening with ours?

NEWMAN: Thanks, Shalini. Technical rejection notices can occur for several reasons. FDA applies eCTD validation criteria to all submissions and assigns a severity level to any identified errors.

To avoid the most common technical rejection, keep the following in mind. Include the us-regional.xml file. This file is required and must be present in your submission. Remember to submit files in the correct structure, and do not submit a single standalone file. Submissions must be organized in folders containing the appropriate files and subfolders. And remember to verify the application type and number, and ensure that both match exactly to what is listed on the corresponding FDA forms.

Lastly, submit a complete Form FDA 356h. An incomplete or missing 356h form will automatically be rejected.

Again, those are just some of the common ones that we see, but hopefully that will help avoid the most common issues. Back to you, Shalini.

SEETHARAMAN: Great points, Tyree. Thank you. So, following up on the previous question, this is a good one for Jessica to answer.

Jessica, one of our sponsors noticed that in the eCTD technical conformance guide there is a requirement to notify the district office by letter that our eCTD submission will be submitted to the FDA. How do we contact that office, and is email contact available?

BOEHMER: Thank you, Shalini. This is a great question that's come up from time to time. For applications submitted to CBER, a field copy certification is not required. CBER acts as the home district for pre-license inspections of CBER-regulated products, so there's no need to send a field copy certification. Back to you, Shalini.

SEETHARAMAN: Thanks, Jessica. Okay, we are moving on to our next question, and this one is for Nadia.

This sponsor is planning to submit their first BLA in Q4 2026. Can you walk through what an application orientation meeting is, what its purpose is, and what the sponsor should expect in terms of format, timing, and who typically participates from both the sponsor and OTP sides?

WHITT: Thanks, Shalini. Congratulations on your upcoming BLA. This is a great one to walk through.

An application orientation meeting, or AOM, is a meeting we hold with sponsors before the filing decision is made. The main purpose is to help our review team get oriented to your application — understanding how it's organized and where the key components are located — so reviewers can get up to speed quickly.

In terms of what we're looking for from you during the meeting, we don't need a deep dive into your studies or a lengthy presentation on the science. What's most helpful is a straightforward walkthrough of where things live in the file.

For example, where the clinical study reports are, where the CMC information is, how the CMC information is organized, or how the modules are structured. Think of it as a roadmap for our reviewers rather than a defense of your data.

Format-wise, it's typically a teleconference or video conference and tends to be fairly informal. On our end, you can generally expect to hear from the project manager and review team leads across disciplines. On your end, we'd encourage you to bring whoever is leading the BLA effort — like your regulatory lead, your CMC lead, and clinical lead — at a minimum, so we can have a productive conversation.

We typically reach out to schedule the meeting once your full application is received, so you don't need to do anything special to request it. Just be ready with that high-level roadmap of your submission. Back to you.

SEETHARAMAN: Thanks, Nadia. Sticking with the theme of BLA submissions, this question is for Tyree.

As we prepare for our BLA submission later this year, what can we as an applicant do to ensure a smooth filing review and avoid any issues that could lead to a refuse-to-file decision?

NEWMAN: Thanks, Shalini. It's excellent that you are already anticipating how best to proceed at such an early stage. One of the most important things you can do now is make sure your application is complete and well organized before you submit. An application is considered incomplete if you are missing modules, missing required forms like the FDA 356H, and if there are gaps in your CMC or clinical data packages. These are just some of the most common reasons we issue a refuse-to-file decision.

Now, one resource I'd really encourage you to take advantage of is reviewing the discipline-specific CBER filing checklists, which are available online. These checklists can give you a clear picture of what our reviewers are looking at during the filing review. Reviewing those checklists

against your own submission is one of the best things that you can do. Our filing review process is outlined in SOPP 8401, which covers the administrative processing of original BLAs, and our refuse-to-file procedures are covered in SOPP 8404.

Again, these resources are publicly available and worth the read. Beyond that, make sure you're submitting in eCTD format, that your study data is in the proper CDISC format — whether it's the Study Data Tabulation Model or the Analysis Data Model — and that all required certifications are included. Hopefully this is helpful. Back to you, Shalini.

SEETHARAMAN: Great answer. Thanks, Tyree. And before we move on to the next question, I just want to remind our attendees again to keep those questions coming to our email inbox. We'll be switching over to live questions shortly.

So, shifting topics a bit: we started off the town hall talking about pre-BLA meetings, and now we have a few questions about mid- and late-cycle meetings that occur after a sponsor has already submitted their BLA package for review. So, let's move into more detail about those. This question is for Jessica.

What exactly is a mid-cycle meeting or mid-cycle communication, and do sponsors have a right to one?

BOEHMER: Thank you, Shalini. The short answer to the second part of the question is yes, with some nuance. The mid-cycle meeting or mid-cycle communication is a PDUFA commitment that is built into the review process for original BLAs under PDUFA VII, which runs fiscal year 2023 through 2027.

FDA is committed to providing mid-cycle communications for all standard and priority review BLA applications. For standard reviews, this meeting typically happens around five to six months after the application is filed. And for priority reviews, it's closer to two to three months after filing. These aren't open-ended discussions. They're FDA's opportunity to flag significant issues, signal whether an advisory committee might be needed, and also to alert sponsors to potential information requests. So, think of it as a checkpoint, not a meeting for negotiation.

Also, I should note that for applications that are subject to a refuse-to-file decision and then are subsequently filed over protest, those applications filed over protest are not eligible for mid-cycle communications or for late-cycle meetings. Thanks. Back to you, Shalini.

SEETHARAMAN: Well said, Jessica. Thank you. And the next question is for Nadia.

What should sponsors bring to a mid-cycle communication meeting? Is there a briefing package requirement?

WHITT: Well, since a mid-cycle communication is FDA-initiated, you typically don't submit a formal briefing package the way you would for a sponsor-requested meeting. That said, being well-prepared is still important. Have your core team available — like your regulatory, clinical, CMC, and biostatistics leads at a minimum — and make sure everyone is up to speed on where the application stands.

If FDA has already signaled through the review that certain areas are under scrutiny, for instance through information requests, be ready to discuss those specifically. The mid-cycle communication is really an opportunity for open dialogue, so the more prepared your team is to engage, the more you'll get out of it. Back to you, Shalini.

SEETHARAMAN: Thanks so much, Nadia. That actually connects really nicely to the next question, which I think Tyree can answer.

How is a late-cycle meeting different from a mid-cycle communication?

NEWMAN: Thanks, Shalini. While they are similar in a way, as both meetings provide opportunities for the FDA and applicant to keep the lines of communication open through the review cycle, each meeting has a distinct purpose. And just to reiterate what Jessica shared, the mid-cycle communication is essentially a status update. During this meeting, FDA tells the applicant where we are in the review process and discusses any major issues, if any.

The late-cycle meeting, however, by contrast, is a more substantive meeting that may address if there any pending information requests, any major deficiencies noted, the status of inspections, or possibly the need for risk management.

FDA generally schedules late-cycle meetings no later than three months before the PDUFA action goal date for standard reviews, or two months prior for priority reviews. This is the applicant's chance to discuss unresolved questions, anticipated labeling issues, or any other significant outstanding matters before the end of the review cycle. Therefore, it is worth investing the time in preparing for both of these types of meetings. Thank you very much. Back to you, Shalini.

SEETHARAMAN: Thanks, Tyree. So, for our next question, it's for Jessica.

Jessica, can you share more about what topics are typically on the table at a late-cycle meeting?

BOEHMER: Thank you, Shalini. Sure. Expanding on what Tyree shared, late-cycle meetings tend to focus on the essential open issues remaining in the pending BLA review. Some common topics include unresolved clinical or statistical questions; proposed labeling language, particularly indications and risk communications; anticipated post-marketing requirements or post-marketing commitments, PMRs or PMCs; and any outstanding CMC or manufacturing concerns. The late-cycle meeting is a natural venue for PMR or PMC discussions, so come prepared to engage on what post-approval commitments might look like. Thanks, and back to you, Shalini.

SEETHARAMAN: Thanks, Jessica. So, Nadia, I'll pass this one to you.

Who from the sponsor organization should attend mid-cycle and late-cycle meetings?

WHITT: That's a great question. For both mid-cycle and late-cycle meetings, the general principle is to mirror FDA's review team with your own cross-functional representation. That typically means having your regulatory lead, clinical lead, biostatistics, CMC and manufacturing, and pharmacology/toxicology representatives at the table, as applicable to your product. Once you receive the meeting agenda, you'll have a much clearer picture of the specific topics FDA plans to cover, and that should guide your final decision on who needs to be in the room. Use the agenda to make sure the right people are prepared and present.

For the late-cycle meeting in particular, where labeling discussions are likely to be front and center, make sure your regulatory and legal teams are looped in and aligned ahead of time — not just present in the room.

On FDA's side, you can generally expect the review division director, the project manager, and discipline-specific reviewers. So match your team accordingly and come prepared to engage at that level.

And one thing I'd emphasize: quality of discussion matters far more than the number of attendees. Back to you, Shalini.

SEETHARAMAN: Thanks, Nadia. Well said.

Thanks to Nadia, Tyree, and Jessica. Those were all really great answers to help our sponsors prepare for those mid- and late-cycle meetings. Okay, we have just a few more questions here

before we switch over to answering some live questions, so please keep those questions coming. Again, you can see the email at the bottom of the slide: OTPevents@fda.hhs.gov. And we will do our best to answer as many questions as we can.

Okay, moving on. This next question is for Tyree, and I think it's an important question to give some context about what happens specifically in OTP once a sponsor submits a BLA.

This sponsor has spent considerable time and resources preparing their BLA and understanding what goes into putting the package together. What they are less clear on is what happens on CBER's end once it's submitted. Can you walk through how CBER reviews a BLA from the filing through to the final decision, including how the different disciplines coordinate, when a sponsor might hear from you, and what the key milestones are that a sponsor should be tracking on their end?

NEWMAN: Thanks, Shalini. To begin with, that's a great question, and one that we're happy to answer because transparency regarding our process is very important. Once you submit your BLA, the first thing we do is a filing review, which takes about 60 days. This is where we assess whether your application is sufficiently complete to permit a substantive review. If it is, we file it and the review clock starts. If there are deficiencies, we may refuse to file and let you know what needs to be addressed.

Once filed, your application is assigned to a multidisciplinary review team that includes reviewers covering clinical, CMC, nonclinical, pharmacology, statistics, and labeling — of course, depending on your product type. Each discipline reviews their section, but they don't work in isolation, as there is ongoing coordination across the team throughout the review cycle.

Throughout the review, you should expect to receive information requests, or IRs. These can come from any discipline at any point in the review cycle. Understand that these are not a sign that something is wrong, as they are just a part of the normal process. What's more important is that you respond to them promptly and completely, because unresolved IRs can affect our ability to complete the review on time. Your project manager will be your primary point of contact for coordinating those responses.

Now, one thing we want to emphasize: if you are aware of any discrepancies in your submission, please do not wait for us to find them. You should already be evaluating those issues internally and developing a strategy to address and resolve them. Coming to us with a well-thought-out plan demonstrates good faith and puts you in a much stronger position than being reactive. If discrepancies surface during our review and it's clear they haven't been considered on your end,

that could slow things down considerably and raise broader questions about the quality of the submission.

Now, around the mid-cycle point, you'll typically hear from us more formally. This is where we flag any major issues identified so far and give you an opportunity to respond before we get deeper into the review. We'd rather address issues early than sit on them until the end.

Now, if your product warrants an advisory committee meeting, that must be scheduled during the review cycle, and you will be notified well in advance. As we approach the action date, you should also be thinking about post-marketing requirements and commitments. As Jessica spoke to, PMRs or PMCs — PMRs are studies or trials we require by law as a condition of approval, typically to further characterize the safety, efficacy, or the product's performance in specific populations. PMCs are studies you can agree to conduct but are not legally mandated, and both will be clearly communicated to you as part of the approval action, along with the agreed-upon timelines for completion. We take these seriously and will follow up on them, so it's important that you build them into your post-approval planning from the start, not as an afterthought.

Now, towards the end of the review cycle, you'll receive our proposed labeling and any remaining outstanding questions. The goal on our end is to get to a decision — which is either approval, complete response, or otherwise — by the PDUFA goal date. Throughout all of this, again, your project manager is your primary point of contact and can help you navigate through this process. So we encourage applicants to stay engaged, as this works best as a two-way process, and open communication on both sides leads to better outcomes. Thank you, Shalini. Back to you.

SEETHARAMAN: Thanks, Tyree. Well answered. So let's move on to the next question. Okay, we have time for only one last question that was submitted ahead of time before we switch on to live questions. This one is for Jessica.

OTP recently approved an original BLA under the Commissioner's National Priority Voucher (CNPV) program in approximately 60 days from filing — a dramatic departure from the standard 10- to 12-month review timeline. Given FDA's stated commitment to integrating AI into its operations, is OTP or CBER leveraging AI tools to support the review process under CNPV? If so, what types of AI applications are being used? And how does FDA ensure scientific rigor and human oversight are maintained in such compressed time frames?

BOEHMER: Thank you, Shalini. The review team did a fantastic job in meeting the expedited timeline for review of the original BLA. The reviewers put in an enormous number of hours working through a highly complex and resource-intensive review. The speed came from how the

work was structured under the Commissioner's National Priority Voucher, or CNPV, model — with parallel reviews, extensive pre-submission engagement, and a focused multidisciplinary council meeting — not from any reduction in scientific rigor in the review.

AI was part of the process; however, only in a supporting role. It was used to summarize large volumes of data, aggregate information, and help sharpen presentations ahead of the council meeting. The actual scientific thinking, the weighing of evidence, the decisions — all of that was done by the review team. AI helped them work smarter and more efficiently with a dense file, but it didn't do the reviewing. AI is a tool for reviewers, but not a replacement for their judgment in the review. Back to you, Shalini.

SEETHARAMAN: Well said, Jessica. Thank you so much. So, we are moving on to our live Q&A. Let's get to the first question.

The first question is on companion devices. So, I'm going to take this one and give our panelists a breather and time to get their thoughts together for the live Q&A.

The question is: we are developing a cell and gene therapy product that requires a companion delivery device that would be co-developed and co-submitted alongside our BLA. Given that the delivery device would be subject to a separate pre-market review pathway under CDRH, what is FDA's current thinking on coordinating the parallel development and submission timelines between CDER and CDRH? Specifically, we would like to understand how labeling alignment, device-biologics classification determinations, and cross-center review coordination are managed when the device is integral to the safe administration of the biologic, and what steps we should be taking early in the development to avoid downstream review delays.

Having managed a BLA with a companion device, this is exactly the kind of question we want sponsors raising early — not at the pre-BLA meeting, not at the BLA submission, but as early as possible. I cannot stress enough the importance of early interactions via formal meetings with both CBER and CDRH centers to obtain FDA feedback and to avoid issues during the BLA review.

On submission timing, your BLA and the device application need not be submitted simultaneously, but the review timelines need to be coordinated. We can help you think through the sequencing, but again, the conversation with the FDA needs to happen early.

Another important aspect of early interaction: if unsure of whether the device will be regulated, then contact the Office of Combination Products to determine if there is a need to submit a Request for Designation and how your device-biologic product would be characterized.

One thing sponsors should know is this is a coordinated review by the FDA. OTP actively involves the CDRH review team throughout the BLA review process, and we involve them at all milestone meetings. It's not two parallel reviews happening in isolation. But that coordination works best only if the sponsors have engaged with both centers early and aligned their biologic and device development programs right from the outset.

And please, again, I cannot stress enough — come to us early. That's the most important message.

SEETHARAMAN: Okay, so for our next question, we'll move on to Jessica.

Our BLA was approved with Reportable 506B PMRs and Non-reportable 506B PMCs. Please advise how we should submit the progress update on these. Can we send it as a bundle or in one submission?

BOEHMER: Thank you, Shalini. The status update for all reportable 506B PMRs and PMCs must be submitted annually, labeled as "Annual Report - PMR/PMC Annual Report."

It may not contain any other information or updates not related to Reportable 506B PMRs or PMCs. Non-reportable 506B PMCs (or non-506B PMC or CMC PMCs) should be reported annually as a product correspondence, labeled as "Commitment - Correspondence Status Update Submission." They cannot be bundled with reportable 506B PMRs and PMCs. And I should also mention that CMC annual reports and labeling annual reports are submitted labeled as "Annual Report - Changes to an Application."

A great resource to refer to for additional details is SOPP 8413 on post-marketing requirements and commitment-related submissions. Back to you, Shalini.

SEETHARAMAN: Thanks for that answer. Jessica, let's move on to our next question, which is for Nadia.

We are preparing an SPL submission for a BLA involving a gene therapy product and have encountered a situation where a product's route of administration does not appear in FDA's current controlled terminology list. Given that gene therapies often involve novel or uncommon routes of administration, what steps should we take to ensure a compliant SPL

submission, and how should we engage with FDA to resolve this terminology gap before our action date?

WHITT: That's actually a situation we see come up in the gene therapy space, and the good news is that there's a clear path forward — it just requires acting early and on two fronts simultaneously.

The first step is to formally request that FDA add the new route of administration term to the controlled vocabulary list. When you make that request, be specific about why existing terms don't accurately describe your intended route, and make sure to reference your anticipated BLA action date so FDA understands the timeline you're working against.

At the same time — and this is important — request interim guidance on an acceptable placeholder term you can use while that terminology update is being processed. That way, your submission can move forward without being held up waiting for the vocabulary list to be updated.

Both of these requests should go to FDA's SPL coordinators, and make sure your regulatory project manager, your RPM, is looped in as well. Your RPM is really your best point of contact for coordinating across the review divisions and can help escalate if needed. If your action date is imminent, flag that urgency explicitly and ask for an expedited response.

The key takeaway here is: don't wait. The earlier you surface this issue, the more options you have to resolve it cleanly before your action date. Back to you, Shalini.

SEETHARAMAN: Well said. Thanks, Nadia. So, we will move on to our next question, which is for Jessica.

What pre-BLA interactions are recommended for a rolling BLA submission, and is a separate meeting to review topline Phase 3 data recommended before the formal pre-BLA meeting?

BOEHMER: Thank you, Shalini, and thank you to the sponsor that submitted this question. Rolling review, again, is granted only for those applications with RMAT, breakthrough, or fast-track designation granted. So, if you have been granted RMAT or breakthrough therapy designation, you should hold your initial comprehensive meeting as noted in your designation letter. You are also eligible to have Type B meetings during your development program. We highly encourage you to have an end-of-phase meeting and a pre-BLA meeting, and the topline Phase 3 data will be discussed as part of your pre-BLA meeting. Thanks, and back to you, Shalini.

SEETHARAMAN: Great answer. And we will move on to Nadia for the next question.

If a BLA is submitted in a rolling fashion, do the OTP reviewers review each component as it is received, or do they wait until all modules have been submitted?

WHITT: That's a great question. And just to recap from earlier, the BLA is not considered received and the review clock does not start until the final module is submitted. As for whether reviewers look at modules as they come in during a rolling review, that's generally at the discretion of the review team. In practice, early review of submitted modules can help reviewers familiarize themselves with the application, which is one of the key benefits of the rolling review process. It can allow for a more efficient review once the full application is received. Back to you, Shalini.

SEETHARAMAN: Thanks, Nadia. Okay, we'll keep moving. The next question is for Tyree.

Can the agency indicate if there is a BLA checklist or guidance which includes an indication — for example, copies of technical documents — which are required or expected for BLA review?

NEWMAN: Thanks, Shalini. This is a great question. A link to the filing checklist is included in SOPP 8404, which covers refusal-to-file procedures and contains the information necessary to successfully review the BLA. It is included in the resources slide of this town hall. Thank you. Back to you, Shalini.

SHSEETHARAMAN: Thanks, Tyree. Okay, we'll move on to the next question, and this is for Jessica.

Is there a limit to the number of questions that can be submitted in advance of a pre-BLA meeting?

BOEHMER: Thank you, Shalini. This comes up all the time. Yes, 10 questions total, inclusive of sub-questions. So, if you have A, B, C, D as sub-questions, each of those counts. So, 10 questions total — that's the limit. Thanks, Shalini. Back to you.

SEETHARAMAN: Thanks, Jessica. Jessica, you'll be answering the next question as well.

Does FDA recommend face-to-face pre-BLA meetings?

BOEHMER: Thank you, Shalini. Yes, we recommend pre-BLA meetings be held face-to-face, in person, with the review team. We also recommend that end-of-phase 2 meetings be held in person with the review team. This allows for more robust discussion at these important phases of your development. So that's our recommendation. Back to you, Shalini.

SEETHARAMAN: Thank you so much, Jessica. So, we'll move on to Nadia for the next question.

Does FDA have any recommendations regarding submission of a reviewer's guide in section 1.2 of the BLA?

WHITT: Yes, we do recommend including a reviewer's guide in section 1.2, and it can be generally valuable to the review team. A well-prepared reviewer's guide helps our reviewers navigate the application efficiently, particularly for complex submissions like cell and gene therapy products, where the organization of data can be intricate.

At a minimum, a helpful reviewer's guide should provide an overview of the application structure, explain how the modules are organized, highlight where key data and study reports are located, and flag any unique aspects of the submission that reviewers should be aware of upfront. Think of it as giving our review team a roadmap before they dive in. The clearer and more organized it is, the smoother the review process tends to go. Back to you, Shalini.

SEETHARAMAN: Agreed. Thanks, Nadia.

We have received a lot of great live questions, so we are going to stay on for a few more minutes and answer a few more of your questions. The next one is for Tyree.

How typical is it for FDA to respond to a meeting request within the 21-day time frame referenced in the guidance?

NEWMAN: Yes, OTP makes every attempt to respond to meeting requests within 21 days with a Type B pre-BLA meeting request. Thank you. Back to you, Shalini.

SEETHARAMAN: Thank you. The next question is for Jessica.

What is the time frame for filing a supplemental BLA? Can you please clarify supplemental BLA review timelines?

BOEHMER: Thank you, Shalini. Assuming that they are referring to efficacy supplements, these are filed 60 days from receipt — the same as for an original BLA. However, the full review timeline from receipt of the efficacy supplement is a six-month review under priority timeline, or a 10-month review under standard review. Thanks, and back to you, Shalini.

SEETHARAMAN: Okay, we'll move on to the next question, and this is for Nadia.

Can a meeting request be submitted as a "product correspondence" to a BLA and filed accordingly in eCTD, and then subsequently submitted through ESG?

WHITT: Yes, after a BLA is approved, an applicant can submit a meeting request for their licensed product as a product correspondence to the BLA. During the review period, a formal meeting request can be submitted, but it must be submitted as an amendment to the BLA rather than as a product correspondence.

In both cases — whether the product is under review or already approved — submission should be made electronically through the ESG in eCTD format. And if you have any questions about the submission process, I'd encourage you to reach out to CBER's ESUB prep support team. Thank you.

SEETHARAMAN: Thanks, Nadia. Okay, we have two more questions. The next question is for Tyree.

I wanted to reach out to inquire about the timeline for when the FDA will begin accepting biologic license applications in the new ICH M4Q revision 2 format. As we plan our upcoming submissions, it would be very helpful to understand when this new format will be officially accepted so we can ensure our documents are prepared accordingly.

NEWMAN: Thank you, Shalini. Right now, discussions are still ongoing, so we don't have a timeline for when this will be implemented, but as soon as we do, we will of course let you know. Thank you very much. Back to you, Shalini.

SEETHARAMAN: Thanks, Tyree. And for our final question, Nadia, I'm going to let you answer this.

What are the typical questions asked during the pre-BLA meeting? What questions must be included in the pre-BLA meeting to ensure alignment with the agency?

WHITT: That's a great question. I'm going to refer you to a great resource that we have on our website — Interactions with OTP, under the pre-BLA meeting section. This resource will give you additional context tailored to the types of questions asked in pre-BLA meetings. Back to you, Shalini.

SEETHARAMAN: Thanks so much, Nadia. And that would be the end of our town hall.

Thanks to everyone who sent in questions ahead of time. Those were all great questions — we really appreciate it. And we are going to wrap up now.

We would like to end by sharing a few resources, as shown in this slide, all of those resources are searchable on FDA.gov and are available to support you during your product development and application stages. Let's move on to our final slide.

Okay, thank you all for joining. If you have questions or doubts about your submissions, or have submitted meeting requests but not heard back, we encourage you to reach out to your assigned RPM or email OTPRPMS@fda.hhs.gov.

Once again, thank you all for joining and for your questions. We hope you found this town hall informative and helpful. I would also like to extend a thank you to our panelists and the behind-the-scenes folks who helped make today's event a great success. As a reminder, a recording of today's town hall will be posted on fda.gov in the coming days. Have a great day, everyone. Thank you.

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