SUBSTANTIAL EQUIVALENCE

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AGENDA

- **Part I: SE Program Overview**
  - Statutory Authority
  - Standard
  - Regulars vs Provisionals
  - Review Process Phases

- **Part II: SE Program Updates**
  - Unique Identification
  - Letter Language Updates
  - Focusing Scientific Resources
  - Deficiency Letter Response Time
  - Common Issues in SE Reports
  - Performance Goals

SUBSTANTIAL EQUIVALENCE PROGRAM OVERVIEW

STATUTORY AUTHORITY

- The Family Smoking Prevention and Tobacco Control Act authorizes FDA to establish a premarket program to manage submissions related to substantial equivalence. Specifically, section 905(j)(1) states:

  - In general.-- Each person who is required to register under this section and who proposes to begin the introduction or delivery for introduction into interstate commerce for commercial distribution of a tobacco product intended for human use that was not commercially marketed (other than for test marketing) in the United States as of February15, 2007, shall, at least 90 days prior to making such introduction or delivery, report to the Secretary (in such form and manner as the Secretary shall prescribe)--

SUBSTANTIAL EQUIVALENCE STANDARD

- For a determination of substantial equivalence, the manufacturer must demonstrate:
  - that the new product has the same characteristics as the predicate tobacco product;
  - or has different characteristics than the predicate tobacco product but the information submitted demonstrates that the new product does not raise different questions of public health

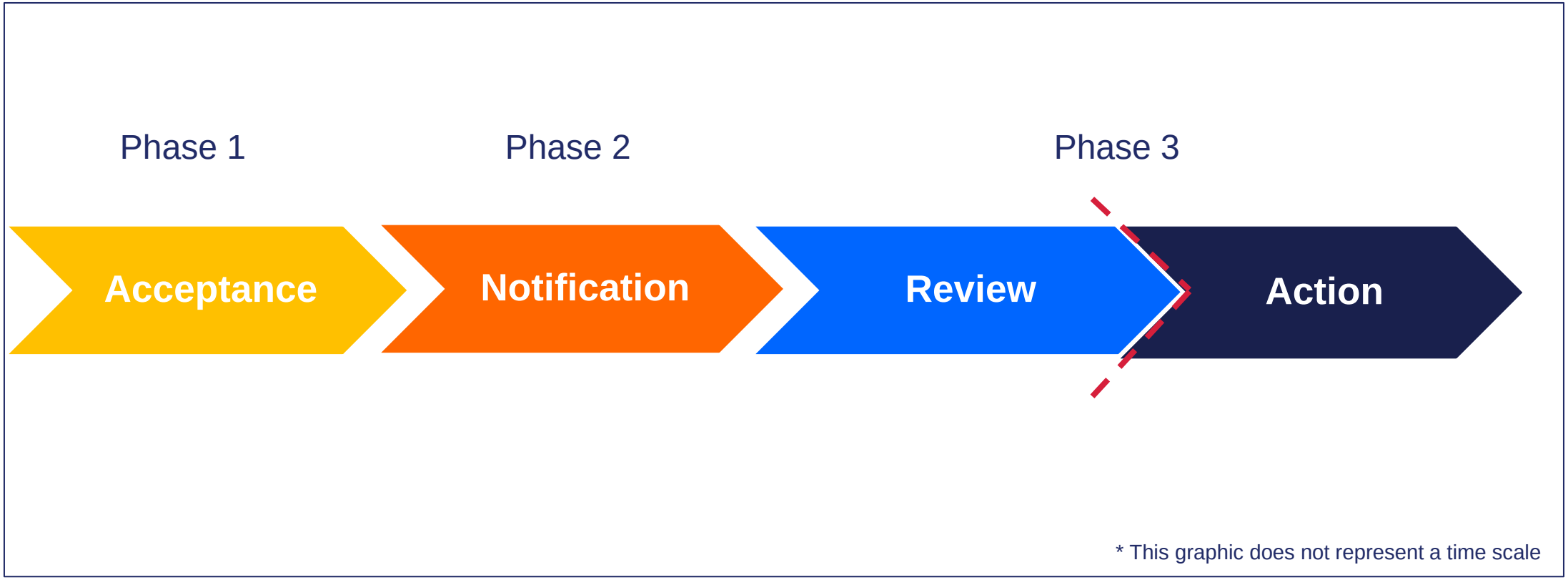
- This means that products brought to market through this pathway will not present more harm to public health than an eligible predicate tobacco product

REGULARS AND PROVISIONAL SE REPORTS

- Regular SE Reports are applications for new tobacco products that require a marketing authorization prior to being introduced to the U.S market.

- Provisional SE Reports are applications for new tobacco products that meet the following statutory criteria:
  - SE Reports were submitted by March 22, 2011, and
  - The products were introduced or delivered for introduction into interstate commerce for commercial distribution in the United States after February 15, 2007, and prior to March 22, 2011.

OVERVIEW OF THE SE PROCESS



SE REVIEW PROCESS

- **Phase I: Acceptance**
  - Step 1: *Application Received* -- FDA receives and processes the application.
  - Step 2: *Acceptance Review*-- FDA reviews the tobacco SE Report to determine if it is under jurisdiction and contains mandated items.
  - Step 3: *Public Health Impact Review* -- All provisional SE Reports have also received a public health impact (PHI) review to determine their order in the review queue.

SE REVIEW PROCESS

- **Phase II: Notification**
  - Step 4: *Predicate Determination* -- FDA conducts a review to ensure the predicate tobacco product is eligible.
    - A tobacco product that was commercially marketed (other than for test marketing) in the United States as of February 15, 2007

OR

    - A product previously found to be substantially equivalent by the FDA and in compliance with the requirements of the FD&C Act

SE REVIEW PROCESS

- **Phase III: Review**
  - Step 5: *Review* – Generally SE Reports are assigned a chemistry, toxicology, engineering and environmental reviewer. Additional scientific evaluation can include social science, addiction, and clinical.
    - If necessary, a deficiency letter will be issued.
  - Step 6: *Final SE Determination* -- FDA determines whether the new tobacco product is substantially equivalent (SE) or not-substantially equivalent (NSE) to a predicate product.

SE REVIEW PROCESS

- **Phase III: Action**
  - Step 7: *Environmental Assessment* – If the SE Report has been found SE from a scientific perspective and additional information is needed, the applicant receives a letter requesting the additional information.
  - Step 8: *Compliance Review* – For Regular SE Reports FDA must determine that the new tobacco product is in compliance with the requirements of the FD&C Act.
  - Step 9: *Courtesy Call* – Once the final TPL and order letter is signed the RHPM will contact the applicant and offer a courtesy copy via email.
  - Step 10: Website *Posting* – The final TPL review and order letter are posted to the FDA website.

PROGRAM UPDATES

SE PROGRAM UPDATES

I. Unique Identification

II. Letter Language Updates

III. Focusing Scientific Resources

IV. Deficiency Letter Response Time

V. Common Issues in SE Reports

VI. Performance Goals

I. UNIQUE IDENTIFICATION

- Over the past couple of years we have provided applicants an opportunity to amend their SE Reports to provide unique identification of the predicate and the new tobacco products.
- TPLs posted on the CTP website provide numerous examples of unique identification of both predicate and new tobacco products for a variety of categories and sub-categories.
- Regulatory Health Project Managers have provided guidance to applicants seeking to better understand how to identify the new and predicate tobacco products.

II. LETTER LANGUAGE UPDATES

- Based on stakeholder feedback, the following updates have been made to our correspondence:
  - Stated the purpose of the correspondence in first paragraph
  - Used plain language where possible
  - Clarified how to submit amendments
  - Removed duplicative language
  - Clearly identified response due dates where applicable
  - Included RHPM email address for ease of communication
  - Visibly identified deficiencies versus requests for information

II. LANGUAGE UPDATES: NOTIFICATION LETTER

We expect to begin our scientific review of all information contained in your SE Report/Reports, including amendments received within 180 days from the date of this letter. We are not obligated to review any amendments received after we begin scientific review. We will determine if information in late amendments will be incorporated in the current review cycle. The Office of Compliance and Enforcement (OCE) assists the Office of Science with certain aspects of SE Reports. OCE may contact you to request additional information.

→ PURPOSE

We expect to complete each cycle of scientific review within 120 days from the scientific review start date. If a review cycle ends with us issuing a Deficiency letter, we expect to provide you with 180 days to respond to the letter. We believe this timeframe will be sufficient for response and do not intend to provide an extension of time.

→ EXPECTED RESPONSE DUE DATE

If you choose to amend your SE Report/Reports, your information should be sent as a single submission with a cover letter that includes the following text in your subject line: **Amendment for** Insert STNs. When responding, we request that your submission include consecutively numbered pages and be organized as follows:

- If responding to requests for information:
  - List each letter to which you are responding.
  - Submit data as an appendix or appendices and reference the appropriate appendix/appendices in your response.
  - Submit publications as an appendix or appendices and reference the appropriate appendix/appendices in your response.
- If resubmitting information (e.g., tables) to correct earlier omissions/errors, clearly identify what information has been revised. FDA will consider that new information to supersede the information provided in the original submission, except for measured values (e.g., test data, HPHC data). For measured values, applicants should provide rationale for why the updated data are appropriate for consideration. If rationale is not provided, measured values will be combined with previous measured values for evaluation.
- If providing new information, clearly identify what is being submitted.

→ AMENDING SE REPORTS

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If you have any questions, please contact Insert RHPM name, credentials Regulatory Health Project Manager, at Insert phone number or Insert email address@fda.hhs.gov.

→ RHPM CONTACT INFORMATION

III. FOCUSING SCIENTIFIC RESOURCES

- In July 2017, FDA Commissioner Scott Gottlieb, M.D. noted CTP would examine its existing approach to the review of the approximately 2,500 remaining provisional SE Reports.
  - In response to this directive CTP took the following actions:
    - To date removed from review (RFR) an estimated 1200 provisional SE Reports.
      - *A complete list is available on the CTP Website*
    - CTP continues to review approximately 1000 remaining provisional SE Reports that are more likely to raise different questions of public health.

III. FOCUSING SCIENTIFIC RESOURCES

- Provisional SE Reports Removed from Review (RFR) will remain with this status unless one of the following occurs:
  - The new tobacco product that is the subject of the provisional SE Report is also the subject of another pending application submitted by the same manufacturer (e.g., an MRTP application, SE Report, or an Exemption Request) .
  - FDA receives new information (e.g., from inspectional findings) suggesting that the new tobacco product that is the subject of a provisional SE Report is more likely to have the potential to raise different questions of public health than previously determined.
  - FDA has reason to believe that the new tobacco product was not introduced or delivered for introduction into interstate commerce for commercial distribution in the United States after February 15, 2007, and prior to March 22, 2011.

III. FOCUSING SCIENTIFIC RESOURCES

As part of the RFR process, CTP decided to focus its resources on provisional SE Reports with the following proposed changes:

- Non-conventional new product
- New or predicate product is inadequately characterized
- New product category is different from predicate product category
- >5% increase in total alkaloids or bases
- Design changes that may increase HPHC quantities
- Increase in HPHCs
- >30% blend change

IV. DEFICIENCY LETTER RESPONSE TIME

- **Pre- October 1, 2018:**
  - Applicants received either Advice/Information Request letters or Preliminary Finding letters (also known as “Deficiency letters”). These letters had a response time of 60 days or 30 days respectively.

- **Post- October 1, 2018:**
  - Applicants will receive a “Deficiency Letter” with a response due date of up to 180 days
  - FDA does not intend to grant additional extensions of time to respond to deficiency letters.
  - **For Provisionals Only:** Notification letter will provide applicants 180 days to amend their pending SE Reports.

IV. DEFICIENCY LETTER RESPONSE TIME

RHPMs monitor CTPs submission system to ensure amendments are received on time.

- If amendments are received before 180 calendar days:
  - The RHPM will process the amendment to ensure the applicant responded to all deficiencies.
  - If it's a complete response (i.e., a response was provided for every deficiency), scientific review will commence early.
  - If it remains an incomplete response CTP will wait until the 180 day response time has lapsed and initiate scientific review on day 181.

- If amendments are received after 180 calendar days:
  - CTP does not intend to review late amendments, however this information may be incorporated in the next scientific review cycle, if applicable.

V. COMMON ISSUES IN SE REPORTS

- As of October 1, 2018 FDA started issuing revised:
  - Acknowledgement Letter
  - Notification Letter

- The new letters include appendices with common issues FDA has identified in previous SE Reports for the specific tobacco product category and sub-category.

  - Information provided is general and not specific to the new and predicate tobacco products within the SE Report

  - This information is not reflective of a scientific evaluation of the submitted SE Report

V. COMMON ISSUES: APPENDIX SAMPLE

APPENDIX A

Information to Consider for Cigarettes

The information included in this appendix reflects deficiencies frequently seen in previous SE Reports for cigarettes that FDA has reviewed. It should be noted that, although this information is specific to cigarettes, some of it may not be applicable to your SE Report. To the extent that it is applicable, you can use this information to determine whether your SE Report should be amended prior to FDA's review of your SE Report.

Identification of the New and Predicate Tobacco Products

Unique identification is an important element for new and predicate tobacco products. Unique identification is necessary so that FDA can accurately identify which products should be compared for a determination of substantial equivalence. Without unique identification, it is difficult for FDA to begin a scientific comparison to determine substantial equivalence.

Unique identification may include, but is not limited to, attributes such as brand, name, descriptors, packaging, size, count, and unit of use. You should provide the following information to uniquely identify the new and predicate tobacco products:

- The manufacturer
- Product name, including the brand and subbrand
- Product category, product subcategory, and product properties, as provided in Table 1

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V. COMMON ISSUES: APPENDIX SAMPLE CONT..

APPENDIX A

Table 1. Cigarette Subcategory and Corresponding Product Properties

Cigarette Subcategory	Product Properties
Combusted, Filtered	• Package type (e.g., hard pack, soft pack, clam shell) • Package quantity (e.g., 20 cigarettes, 25 cigarettes) • Length (e.g., 89 millimeter (mm), 100 mm) • Diameter (e.g., 6 mm, 8.1 mm) • Ventilation (e.g., none, 10%, 25%) • Characterizing Flavor(s)[1] (e.g., none, tobacco, menthol) • Additional properties needed to uniquely identify the tobacco product (if applicable)
Combusted, Non-filtered	• Package type (e.g., hard pack, soft pack, clam shell) • Package quantity (e.g., 20 cigarettes, 25 cigarettes) • Length (e.g., 89 mm, 100 mm) • Diameter (e.g., 6 mm, 8.1 mm) • Characterizing Flavor(s) (e.g., none, tobacco, menthol) • Additional properties needed to uniquely identify the tobacco product (if applicable)
Combusted, Other	• Package type (e.g., hard pack, soft pack, clam shell) • Package quantity (e.g., 20 cigarettes, 25 cigarettes) • Length (e.g., 89 mm, 100 mm) • Diameter (e.g., 6 mm, 8.1 mm) • Ventilation (e.g., none, 10%, 25%) • Characterizing Flavor(s) (e.g., none, tobacco, menthol) • Additional properties needed to uniquely identify the tobacco product (if applicable)

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V. COMMON ISSUES: APPENDIX SAMPLE CONT..

Use of a Predicate Tobacco Product You No Longer Manufacture

If you no longer manufacture the predicate tobacco product, you should still fully characterize the predicate tobacco product in order for FDA to determine all differences in characteristics between the new and predicate tobacco products. Data on the predicate tobacco product may be required to demonstrate substantial equivalence of the new tobacco product. Some potential options for obtaining data on the predicate tobacco product include:

1. Manufacture the predicate tobacco product at present day, consistent with the product composition and design specifications in place at the time the predicate tobacco product was originally manufactured. In this case, design parameter data should be accompanied by documentation demonstrating that the manufacture of the predicate tobacco product at present day is reflective of the predicate tobacco product at the time of original manufacture. Where any difference exists between the present-day predicate tobacco product design parameters, components, or constituents and the original predicate tobacco product, those differences should be noted, and the present-day predicate tobacco product will be considered a surrogate tobacco product (see "Use of a Surrogate Tobacco Product" below).

2. Identify another, currently available tobacco product with design parameters, components, and constituents similar to the predicate tobacco product. This tobacco product will be considered a surrogate tobacco product (see "Use of a Surrogate Tobacco Product" below). Where any difference exists between the surrogate tobacco product design parameters, components, or constituents and the predicate tobacco product, those differences should be noted.

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VI. PERFORMANCE GOALS

Performance Measure	FY17 Goal	FY17 Actual	FY18 Goal	FY18 Actual	FY19 Goal	FY20 Goal	FY21 Goal	FY22 Goal
Regular SE Reports								
Issue ACK, RTA, or Withdrawal ACK letter within 21 days	70%	95%	80%	92%	80%	80%	80%	80%
Issue A/I, PFind, Cancellation, Closure, SE or NSE order letter within 90 days	70%	73%	80%	96%	80%	80%	80%	80%
Provisional SE Reports								
Issue Withdrawal ACK Letter within 21 days of receiving Withdrawal Request	n/a	n/a	n/a	n/a	50%	60%	70%	80%
Issue A/I, PFind, Cancellation, Closure, SE or NSE order letter within 120 days of scientific review commencing	n/a	n/a	n/a	n/a	50%	60%	70%	80%

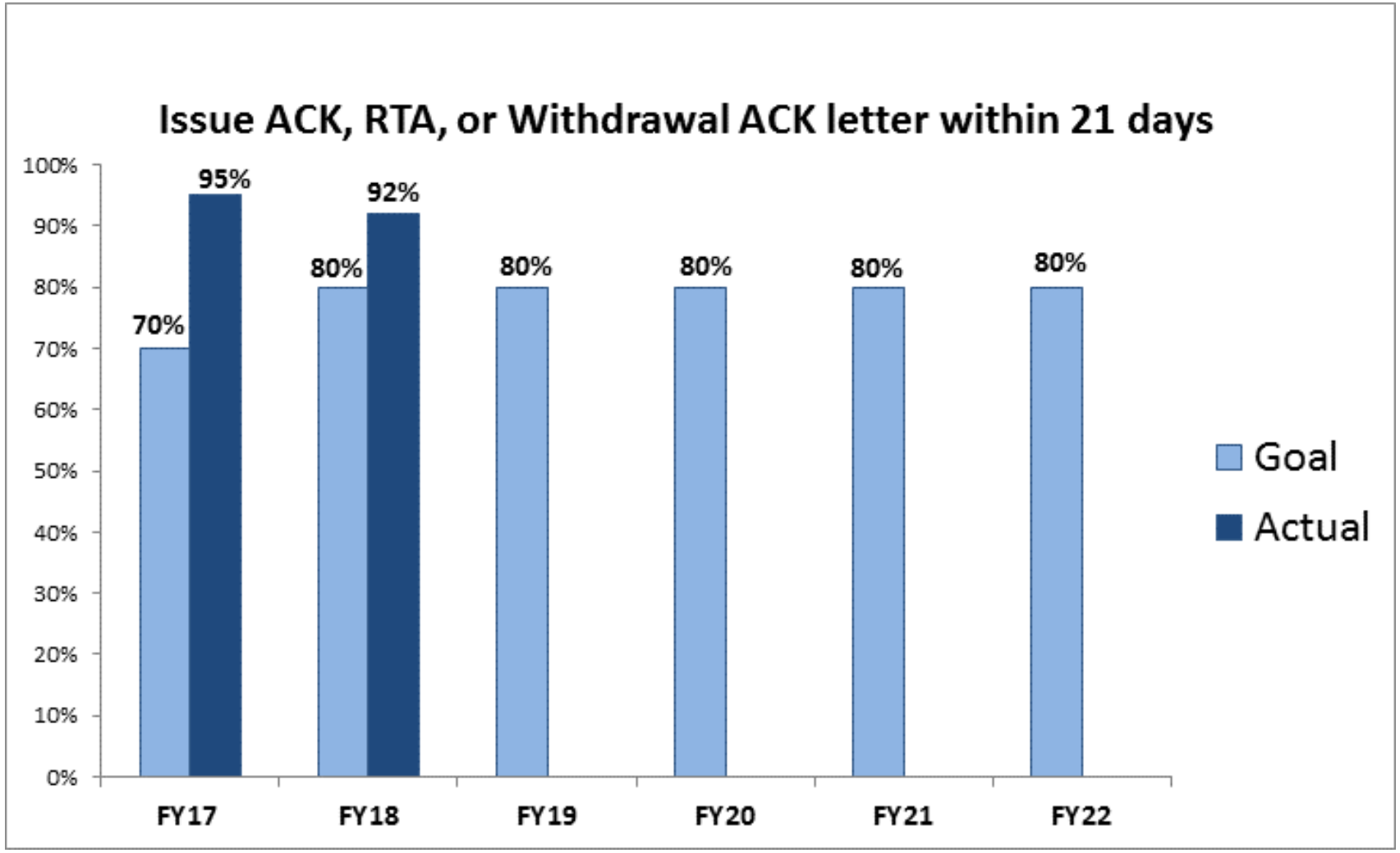
[1] ACK and RTA is 21 days from date original SE Report received. Withdrawal ACK is 21 days from date withdrawal amendment is received. ACK= Acknowledgement letter. RTA= Refuse To Accept letter

[2] 90 days from date original SE Report received. 90 days from date complete response to A/I or PFind letter received, or date response to A/I or PFind letter is due, whichever is sooner.

[3] 21 days from date withdrawal amendment is received.

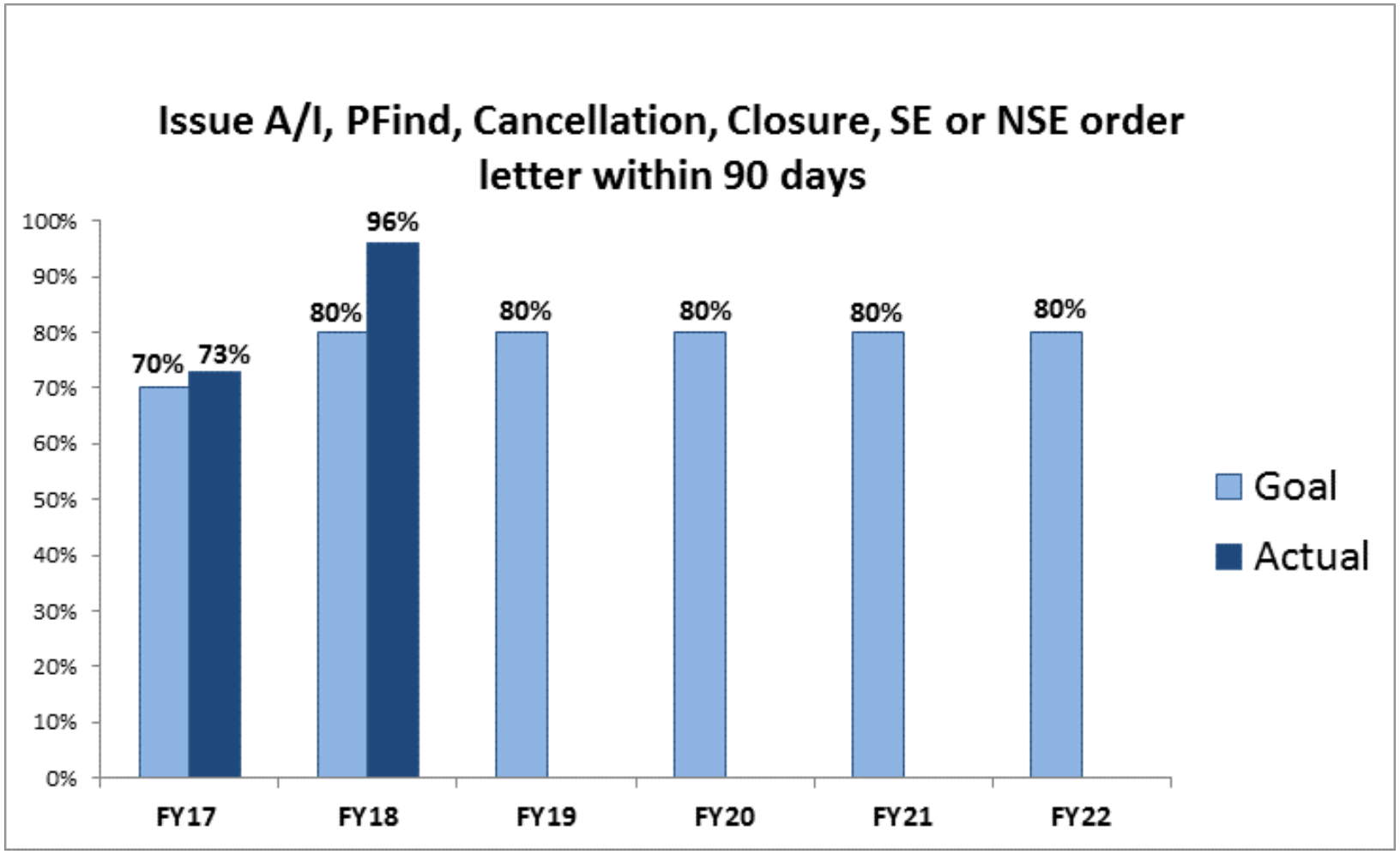
[4] 120 days from date review of original SE Report expected to start (i.e., as indicated in the Notification letter). 120 days from date complete response to A/I or PFind letter received, or date response to A/I or PFind letter is due, whichever is sooner

VI. PERFORMANCE GOALS: REGULAR SE REPORTS



* For fiscal year (FY) 18 the cohort is still open, updated numbers will be made available in early 2019

VI. PERFORMANCE GOALS: REGULAR SE REPORTS

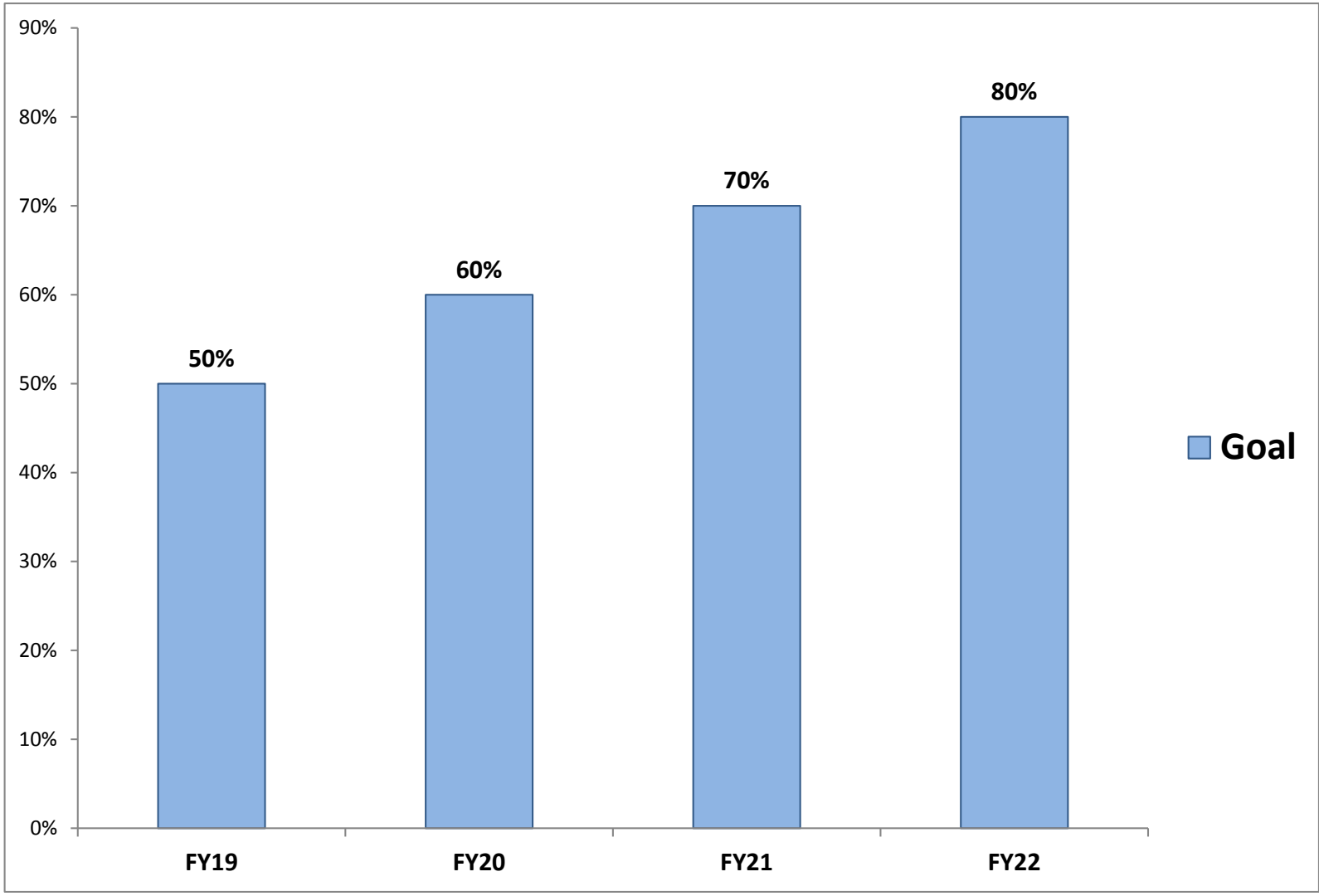


* For fiscal year (FY) 18 the cohort is still open, updated numbers will be made available in early 2019

VI. PERFORMANCE GOALS: PROVISIONAL SE REPORTS

- Issue Withdrawal ACK Letter within 21 days of receiving Withdrawal Request

- Issue A/I, PFind, Cancellation, Closure, SE or NSE order letter within 120 days of scientific review commencing



RESOURCES

Your assigned RHPM is your point of contact and can help with:

- General inquiries about premarket pathways, application submission, & review process
- Inquiries about useful resources available for manufacturers on CTP's website
- Clarification of regulatory requirements communicated through guidance & regulations
- Clarification on FDA's Deficiency letter
- Providing reference for scientific findings noted in FDA's Deficiency letter
- Inquiries about the process for holding formal meeting with FDA

RESOURCES

- How to determine which pathway is for you
  - https://www.fda.gov/TobaccoProducts/Labeling/TobaccoProductReviewEvaluation/ucm20027142.htm
- RFR List and announcements
  - https://www.fda.gov/TobaccoProducts/NewsEvents/ucm583226.htm
- TPL Site
  - https://www.fda.gov/TobaccoProducts/Labeling/TobaccoProductReviewEvaluation/ucm339928.htm#2
- Performance Measures website
  - https://www.fda.gov/TobaccoProducts/Labeling/TobaccoProductReviewEvaluation/SubstantialEquivalence/ucm475489.htm
- General Inquiries
  - AskCTP@fda.hhs.gov

QUESTIONS?