Update on Review of Substantial Equivalence Reports (SE Reports)

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April 10, 2013

Outline

- Substantial Equivalence Overview & Process
- Prioritization of SE Reports for scientific review
  - Regular and provisional SE Reports
- Common deficiencies in regular SE Reports

Substantial Equivalence Overview

- Outlined in the Food Drug and Cosmetic Act (FD&C Act)
  - Section 910
  - Section 905(j)
- Final Guidance for Industry issued on January 5, 2011
  - To clarify what industry should include to demonstrate a scientific finding of substantial equivalence
- Draft Guidance for Industry issued September 2011
  - To clarify frequently asked questions FDA had received around substantial equivalence

SE Review Process – Phase 1

- Submitted to DCC and sent to OS for RHPM Assignment
- RHPM performs jurisdiction review and acknowledges report
- RHPM performs administrative review for completeness and if deficient, issues an advice/information request (30 day response)
- Upon receipt of applicant response, RHPM performs a second administrative review to determine if any deficiencies remain

SE Review Process – Phase 2

- RHPM sends notification letter to applicant
  - Provides projected start date of scientific review
  - Allows applicant to amend the SE Report prior to the start of scientific review
- RHPM sends a request to OCE for grandfathered determination (if applicable) of predicate tobacco product

Stand alone Grandfathered Submissions

- Voluntary submission
- A stand alone submission should reflect the same information needed for a grandfathered determination performed under SE review
- Draft Guidance entitled, “Draft Guidance for Industry: Establishing that a Tobacco Product was Commercially Marketed in the United States as of February 15, 2007”

SE Review Process – Phase 3

- Scientific review commences
  - Reviewers assigned as appropriate
    - Depending on contents of report and on previous review findings
- Conclusion of review triggers a letter
  - Scientific advice/information request letter (recent letters have requested a response of 60 days)
  - Preliminary Finding letter (recent letters have requested a response of 30 days)
  - Order letter (either SE or NSE)

Prioritization of SE Reports for Scientific Review

Types of SE Reports

- Provisional Reports
  - New tobacco product introduced into commercial distribution 2/16/07-3/21/11; AND
  - SE Report submitted by 3/22/11
- Regular Reports
  - Does not fit criteria for provisional reports

Regular SE Reports: Prioritization for Scientific Review

- Discussed in April 24, 2012 webinar
  - Has taken priority over provisional reports
    - Need an order finding new tobacco product SE to legally market product in United States
- Reviewed in first-in-first-reviewed order

Provisional SE Reports: Prioritization for Scientific Review

- First-In-First-Reviewed would not be practical or appropriate
  - A very large number of provisional SE Reports received on same day

Provisional SE Reports: Prioritization for Scientific Review

- Prioritization based on Public Health Impact (PHI) Tiering
  - The new tobacco products that are the subject of provisional SE Reports are currently being marketed
  - In order to protect public health, products with the greatest potential to raise different questions of public health are being given higher priority in the review queue

Provisional SE Reports: Prioritization for Scientific Review

- Prioritization based on Public Health Impact (PHI) Tiering
  - PHI review to assess potential of new product raising different questions of public health
  - Performed by CTP scientists but *not* a complete scientific review for substantial equivalence
  - SE Reports in the highest PHI tier enter the review queue first

Provisional SE Reports: Steps for PHI Tiering & Scientific Review

- Administrative A/I letters issued
- PHI review of provisional SE Reports for tier assignment
- After SE Reports in highest PHI tier determined, process same as regular SE Reports
  - Notification letter issued
  - Scientific review begins

Factors Assessed for PHI Tiers

- Is the new product a non-conventional product?
- Inadequate characterization of either the new or predicate tobacco products
- Difference in product category between the predicate and new tobacco products

Common Deficiencies Found in Regular SE Reports Reviewed to Date

Scope

- Deficiencies observed in multiple SE Reports from different tobacco product manufacturers
  - Based on completed scientific reviews by FDA
  - Have been communicated to manufacturers
  - Significant deficiencies in nearly all SE Reports reviewed to date

Scope

- Deficiencies presented in webinar may not be applicable to all SE Reports reviewed by FDA

- Will not discuss deficiencies unique to individual manufacturers or specific product types

Scope

- Will discuss some deficiencies discussed in August 2012 webinar
  - All deficiencies discussed in August 2012 are still common
- Limiting current webinar to product composition and design deficiencies
  - Represent some of the most common deficiencies

Scope

- There are other deficiencies not being discussed during current webinar
  - List of deficiencies during current webinar is not meant to be all-inclusive

Incomplete Product Identification

- Need to clearly identify new and predicate products
  - Product name (brand/subbrand)
  - Package type
    - e.g., box, soft pack
  - Package size
  - Unique identification numbers
    - e.g., SKU, UPC, internal identification code

Missing Ingredient Information

- Incomplete ingredient listing

- Ingredient name, quantity, and function provided, but not fully identified
  - Tobacco types stated but no further information (e.g., differentiating different recon. tobacco, grades)
  - Purity (e.g., grade, certificate of analysis)

Missing Ingredient Information

- Quantities stated as percentages
  - Inadequate to determine actual quantities found in products
- Discrepancies in ingredient listings
  - Different sections of SE Report state different quantities
  - Ingredient quantities do not appear accurate

Missing Design Parameters

- Providing some examples but not all-inclusive list
  - Product weight
  - Filler weight
  - Cut width
  - Paper length
  - Paper width
  - Adhesive width

Missing Design Parameters

- Examples
  - Cigarette/tube length
  - Cigarette/tube circumference
  - Cigarette/tube diameter
  - Cigarette/tube weight
  - Base paper basis weight
  - Base paper porosity
  - Band porosity
  - Band width & space

Missing Design Parameters

- Examples
  - Filter pressure drop
  - Filter efficiency
  - Filter length
  - Filter ventilation
  - Filter density
  - Filter draw resistance

Missing Design Parameters

- Examples
  - Puff count
  - Cigarette draw resistance
  - Tobacco rod packing density
  - Plug wrap porosity
  - Tipping paper length
  - Oven volatiles/moisture

Other Product Design Issues

- Missing product schematics
- Unclear whether reported values are targets, tolerance limits, or measured values
- Discrepancies in design parameters
  - Different sections of SE Report state different values
  - Design parameters are not consistent with each other

Missing Harmful and Potentially Harmful Constituents (HPHCs)

- Many SE Reports have not included any HPHC data
- Aids review when new product has differences in characteristics from predicate product
  - e.g., blend change, design change, addition of new ingredients
  - e.g., polycyclic aromatic hydrocarbons (PAHs) or tobacco-specific nitrosamines (TSNAs) may be useful

Missing Harmful and Potentially Harmful Constituents (HPHCs)

- Smoke constituents have been reported under one smoking regimen
  - Can better evaluate differences in characteristics if intense *and* non-intense regimens used

Overarching Deficiencies

- Explanation and supporting data were not adequate to explain why differences in characteristics do not raise different questions of public health
- Incomplete information to evaluate submitted data
  - e.g., analytical method, means & variance, number of replicates

Summary

Five most common deficiencies related to product composition & design found in the regular SE Reports reviewed to date

Deficiency	% SE Reports
Clarification of ingredient listings	94%
Missing HPHC data	87%
Missing design parameters	85%
Clarification of design parameter information	78%
Missing packaging information	61%

Questions?

If you submitted an SE Report,
contact your assigned regulatory health project manager

If you have not submitted an SE Report,
contact the CTP Call Center

1-877-287-1373 (9:00 a.m. – 4:00 p.m. ET)
AskCTP@fda.hhs.gov

For further information, visit our website

www.fda.gov/TobaccoProducts/ResourcesforYou/ForIndustry/ucm238891.htm