

United States Food and Drug Administration  
Adverse Event, Product Experience, and Safety Reporting –  
Electronic Submissions

OMB Control No. 0910-0645

## **Non-Substantive Change Request for CTP Safety Reporting Portal Questionnaires**

The Food and Drug Administration, Center for Tobacco Products (CTP) is seeking OMB approval of non-substantive changes to OMB Control No. 0910-0645. This collection supports adverse experience (health and product problem) reporting associated with FDA-regulated tobacco products to CTP’s [Safety Reporting Portal](#) (SRP) tobacco RQs (i.e., “rational questionnaires”: “TPR<sup>1</sup>” or “Tobacco product report” and “TIR”<sup>2</sup> or “Tobacco Investigator Report”).

The previous set of OMB-approved changes (approval date 5/21/2020, ICR Reference number 202005-910-005) to these SRP tobacco RQs were implemented and released to the field 10/17/2020, with the exception of the mobile version (subset of questions from the TPR questionnaire formatted for mobile devices) which continued in development.

As summarized below, attached are proposed modifications to the SRP’s rational questionnaires for tobacco products. We believe the proposed revisions improve the clarity, internal consistency and utility of the information being collected, thus enhancing CTP’s public health surveillance for new and existing safety signals. Adverse experience reporting to the SRP for tobacco products continues to be voluntary. We believe the changes have a net zero effect on the burden. CTP is planning a potential release date of October 1, 2021.

### **Summary of the Change Request**

In summary there is one new optional question unique to the tobacco industry (on manufacturer type) and one new required question, unique to researchers and manufacturers (on MedDRA version freezing). Two existing optional questions for researchers are planned to become required questions. In both TPR and TIR there are:

- Five new optional questions plus resurrection of one previously approved/retired question in the problem summary section; four on background health that will present to all types of submitters and two that will present only to submitters of health problems.
- Ten questions on tobacco product parts have been reduced to one question, now showing for eight tobacco product types.
- Changes to approximately 15 question stems or response values for clarity and inclusiveness

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<sup>1</sup> The TPR continues to be designed for consumers/concerned citizens and healthcare professionals (who may submit as anonymous or identified guest or as registered account holders) and manufacturers (who must submit as registered account holders). The 2020 version currently in the field is “TPRv4”. The proposed 2021 version is “TPRv5”.





<sup>2</sup> The TIR continues to be designed for researchers (as identified account holders). The 2020 version currently in the field is “TIRv3”. The proposed 2021 version is “TIRv4”.

- Changes to the format of two questions from free text to search and select.
- Relocation of two existing questions to decrease the frequency of their display to each submitter.
- Changes to multiple business rules and changes or additional instructions to prevent or decrease reports bearing internal inconsistencies.
- Retitled two main sections (one in TPR and one in TIR) and two subsections (in both TPR and TIR)
- Improved instructional language throughout

As in last year’s application, the mobile view of the TPR continues to contain a subset of questions from the desktop TPR that are formatted for display on mobile devices. The mobile view is only available to guest (not registered account holder) submitters and uniquely requires to uploaded at least one image before submission – suggested to be an image of the tobacco product or label.

The two optional two-question evaluation surveys are unchanged.

**Table of Attachments**

Document Name	Document Reference name as Used below	Document Description	# of pages
CTP 0910-0645 SRP TPRv4 changes for TPRv5.pdf  Rev CTP 0910-0645 SRP TPRv4 changes	TPR attachment	This file shows the existing 2020 released Tobacco Product Report, TPRv4 questionnaire, marked up with changes proposed for TPRv5. The file shows questions presented to a guest consumer submitter reporting about an electronic cigarette - the most common TPR report type received by CTP.	28
CTP 0910-0645 TIRv3 changes for TIRv4.pdf  Rev CTP 0910-0645 SRP TIRv3 changes	TIR attachment	This file shows the existing 2020 released Tobacco Investigator Report, TIRv3 questionnaire, marked up with changes proposed for TIRv4. The file shows questions presented to an account holder researcher reporting about a cigarette - the most common TIR report type received by CTP.	29
CTP 0910-0645 SRP TPRM1 for 2021.xlsx  CTP 0910-0645 SRP TPRM1 for 2021.xlsx	Mobile attachment	This workbook provides CTP’s objectives for the mobile view in the “Objectives” tab and lists the subset of questions from TPRv5 to be included in the mobile view in the “Mobile Fields” tab.	
CTP0910-0645 SRP Tobacco RQ Evaluation Surveys.pdf  CTP 0910-0645 SRP Tobacco RQ Evaluat	Evaluation attachment	This file describes and shows screenshots of CTPs short optional evaluation surveys for the tobacco RQs.	1

## **Change Request (summarized per section of the RQs):**

### **1. Introduction Section**

- a. TPR edits to the introductory instructional content reveal new data posted for the public at OpenFDA.gov, provide clarifications, and direct acute poisoning events needing urgent medical advice to the Poison Control Centers. [See pp. 3-4/28 in TPR attachment]
- b. TIR edits to the introductory instructional content now include a summary of FDA's regulatory authorities and who should report using the TIR, along with introducing public data available at OpenFDA.gov . It also contains the same table shown in TPR listing where and how to report issues that are not appropriate for the SRP. The TPR and TIR introductions are now similar in structure. [See pp. 3-6/29 in TIR attachment]

### **2. Report Information Section (TPR & TIR)**

- a. Expands the list of response values for the optional existing question "Where else did you report this problem?" to assist with identifying duplicate reports within and outside of FDA. [See p. 5/28 in TPR attachment and p. 6/29 in TIR attachment]

### **3. Contact Information Section**

- a. Changed business rules and reworded the question "Are you the person who experienced health problems associated with a tobacco product?" and the dependent question for those who answer no, asking the relationship of the submitter to the person who had the problem, so these will appear and be relevant to those submitting either a health or a product problem to assist FDA's interpretation of the reliability of the reports. Edits simplify the wording. (TPR, TPRM) [See p.6/28 in TPR attachment]
- b. In TPR, for manufacturers, there is one new optional question about manufacturer type for consistency with the set of questions for other submitter types and to assist FDA's understanding of the likely manufacturing processes and resources based on the type of business. [See p.6/28 in TPR attachment]
- c. No changes for TIR. [See p. 7/29 in TIR attachment]

### **4. Problem Summary Section**

- a. Affected Person Subsection questions [See pp.7-8/28 in TPR attachment; pp. 8/29 in TIR attachment]
  - i. Existing required age question – change to business rule that when the unit "years" is selected, the digits value must be 120 or less in whole numbers and cannot be zero
  - ii. Existing optional body weight question– change to business rules assures that the question will show to all ages of affected persons.
  - iii. New optional question collects height, which along with the existing weight question allows CTP to calculate BMI to better understand dose-response relationships
  - iv. Changes to the question on pre-existing health problems
    1. In the TPR

- a) Added 8 response values, listing problems or damage to 4 major organ systems, Allergies, Surgical implants, and Unknown
    - b) Removes “Other” from the list of response values
    - c) The previously dependent optional free text field to explain “other” pre-existing health problems now shows at page load for all submitters and has revised language “Provide details about the pre-existing health problem(s) above or other pre-existing health problems.”
  - 2. In the TIR – this question was previously an open-ended question with a free text response field. Now it will be identical to the TPR question as described above.
- b. Medications and Supplements Subsection [See p. 8/28 in TPR attachment; p.9/29 in TIR attachment]
  - i. Retitle this subsection to “Medications, Supplements and Substances”
  - ii. Redesign the existing optional question on prescription medications, over-the-counter medications, vitamins, and/or supplements taken around the time of the health problem – into two optional questions. Each question is designed as a search and select field (like our main symptoms question) where multiple product names can be entered (one at a time) from a standardized list to facilitate accurate reporting. The value “Other” is included in each response list with a dependent optional free-text response field to explain “Other.” Each list of entries allows the submitter to edit or delete products after they have been entered.
    - 1. New stem for the first question: “Please list the vitamins, minerals, supplements and herbal remedies taken around the time of the problem.” The standardized list is provided from CFSAN’s SRP RQ.
    - 2. New stem for the second question: “Please list the prescription and over-the-counter medications taken around the time of the problem”. The standardized list is provided from CDER’s SRP RQ.
  - iii. Restore a previously OMB-approved (TPRv1) optional two-part question on alcohol use/#drinks per week
  - iv. Move a previously approved optional question on duration of use or exposure to any type of tobacco product, from the (Main) Tobacco Products section, Tobacco Product Use (or Exposure) Details subsection. This prevents the submitter from seeing this question multiple times when they report the use of more than one tobacco product type.
  - v. Add an optional question to describe in free text, the use of or exposure to common substances of abuse. This will facilitate CTP’s analysis of potential root cause and other contributors to AEs given the trend for poly substance use/abuse.
- c. Problem Description Subsection [See pp. 8-11/28 in TPR attachment; pp. 9-12/29 in TIR attachment]

- i. For the “...main symptoms...” question, in TIR and for TPR (manufacturers only), new informational text explains what MedDRA is, requires to select the desired MedDRA version for the report, and adds one required question asking if the submitter is version freezing MedDRA. This new question helps CTP to support the submitter’s versioning practice if they use MedDRA and facilitates CTP’s downstream data management and analysis. [See pp.10-11 in TIR attachment]
- ii. The optional existing seriousness question is reworded for clarity and hidden if the problem type is a product problem only. (TPR, TIR, TPRM)
- iii. Two new optional questions on settings of care and testing/results facilitate analysis of the serious health problem reports we have been receiving for safety signals of lung injuries and seizures associated with ENDS use. For each type of testing, submitters are shown a field where they can detail the specific test(s) and any results known. These questions are hidden if the problem type is a product problem only.
- iv. The optional existing question on treatments is revised for clarity (asks treatments rendered or planned) and inclusiveness (for either use or exposure) and presents a completely revised list of values for relevance. This question is hidden if the problem type is a product problem only.
- v. The existing optional outcomes question has a revised and expanded list of response values to capture information on the trajectory of the health problem. This question is hidden if the problem type is a product problem only. (TPR, TIR, TPRM)

**5. Research Summary Section (TIR) [See pp. 13-15/29 in TIR attachment]**

- a. This section will be unchanged from that approved by OMB in 2020 (TIRv3) at the time we release most other changes detailed herein. However, soon thereafter (and before our next OMB application), we request to make two existing optional questions become required questions: Name of Principal Investigator and Clinical Trial Site where problem occurred or was discovered. This information is needed to support the Office of Compliance and Enforcement’s (OCE) Bioresearch Monitoring (BIMO) site inspections program soon to launch.

**6. Tobacco Products Section (TPR, TPRM) [See pp. 12-22/28 in TPR attachment] or Study Tobacco Products Section (TIR) [See pp. 16-22 in TIR attachment]**

- a. In TPR and TPRM the “Tobacco Products” section is retitled to “Main Tobacco Products”.
- b. The TPR and TIR have been divergent and are now more clearly so. The “Main Tobacco Products” section in TPR and mobile is for all accused products, whereas the “Other Tobacco Products” section in TPR and mobile is for lifetime or additional tobacco exposures thought by the submitter not to play a role in the problem being reported. The “Study Tobacco Products” section in TIR is for reporting all on-study tobacco products, whereas the “Other Tobacco Products” section in TIR is now retitled to “Nonstudy Tobacco Products” consistent with existing instructions. Minor revisions to instructions intend to add clarity on these differences.

7. **Main Tobacco Products Section /Tobacco Product Details Subsection** (TPR, TIR, TPRM) [See pp. 13-21 in TPR attachment; pp. 18-21 in TIR attachment]
- a. The informational link to a description of the various tobacco product types is changed from a link to a custom-designed single-purpose document to the general public link for this purpose at <https://www.fda.gov/tobacco-products/products-guidance-regulations/products-ingredients-components>
  - b. The existing required question on Tobacco Product Types has minor edits to three response value labels (ENDS, Pipe, and Waterpipe) to reflect shifts in consumer vernacular and regulatory product knowledge.
  - c. Changes to existing Flavors Questions – Six tobacco product types previously had one of three different optional flavors questions. We now ask the same optional flavor question with a shortened five-item multiple choice list of responses for all tobacco product types to standardize and simplify the RQs
  - d. Informational text alerting submitters that it is possible to upload product images already existed in four tobacco product types and is now added to the rest (n=14) for consistency.
  - e. The existing optional question “Where is the tobacco product now?” had been removed from most tobacco product types and now will be removed from the remaining three for consistency.
  - f. The existing optional question “How was the product acquired” had a 6-item single choice response list for most tobacco product types but an 8-item list for four tobacco product types. We now standardize the 8-item list for all tobacco product types.
  - g. The existing optional question about manufacturers that bears the search and select field with data from the compliance database (TRLM), will now display the full contact information for the manufacturer as editable. This may assist submitters to find information that may not be in product labeling.
  - h. A subsection of 10 questions on tobacco product parts that had displayed for each of five tobacco product types is replaced by a single open-ended free text response question. (The same open-ended free text response question was used for the E-cigarette product type in the 2020 release). The same free-text question is added to three additional tobacco product types. This standardizes and simplifies the query on parts throughout the RQs.
  - i. In the Tobacco Product Use Details Subsection (for all tobacco product types and all submitter types), there is new boxed instructional text before the two questions on the duration of use of this brand/label and the duration of use of this tobacco product type, requesting logical temporal consistency between the two questions (duration of use of brand/label is usually the same as or shorter than the duration of use of this type of tobacco product) and some bolded text in each question to visually distinguish between the two questions.
  - j. Changes to ENDS Tobacco Product Type Questions (n=4)

- i. Response values are expanded for “What contained the e-liquid within the device?” to reflect marketplace changes and to support the Final Enforcement Guidance on ENDS (USDHHS/FDA/CTP, 2020)
  - ii. Response values are expanded for “Did the e-liquid (as purchased) contain any of the following?” to reflect marketplace changes (e.g., now includes four nicotine values; type unknown, free-base, salts and synthetic) and common product misuse behaviors (e.g., now includes alcohol, street drugs or other substances mixed into the e-liquid).
  - iii. Hides all but five questions for e-liquids in disposable ENDS devices to decrease reporting burden for this growing market segment of ENDS products.
  - iv. Moves (out of Tobacco Product Use (or Exposure) Details section to E-liquid details subsection) and rewords a question on product modification to specifically capture if the e-liquid was modified before use or exposure. This replacement is for clarity.
- 8. **Tobacco Product Section or Study Tobacco Product Section / Tobacco Product Use Details subsection** [See p. 22 in TPR attachment; pp. 21-22 in TIR attachment]
  - a. Minor rewording to most questions to be more inclusive of and logical for nonuser submitters (i.e., changes “use” to “use or exposure”)
  - b. Retitle the subsection to: “Tobacco Product Use or Exposure Details”
  - c. Expanded the values for the existing optional question asking about routes/methods of use to capture environmental exposures and product accidental and intentional misuse
  - d. Bolded some words in two closely worded questions to prevent item misreading
  - e. Clarified wording of two challenge/rechallenge questions to align with MedWatch
  - f. Changed and expanded response values in the frequency of use question to capture both extremes of use and to better discern user trajectories from experimentation to initiation to addiction, drawing from guidance of Pearson et al., 2018, and IARC 2018
  - g. Added one value to the question on following instructions for product use to capture the common lack of available instructions.
  - h. Added instructional text to discourage submitting illogical information in the two questions on duration of use for this brand and for this type of tobacco product
- 9. **Other Tobacco Products Used Section (TPR)** [See pp. 23-25 in TPR attachment]
  - a. Section retitled to “Other Tobacco Products”
  - b. Most questions and instructions now show on page load.
  - c. Minor edits to instructions for clarity
  - d. Delete the initial question, “Has the affected person used other tobacco products (either currently or in the past)”
  - e. Revised list of values for the tobacco product types and subtypes (same as in the Main Tobacco Products section) Replaced the optional question on current use (Yes/No) with an optional trajectory of use question
  - f. Replaced the optional question on current use (Yes/No) with an optional trajectory of use question

- g. Expanded the list of values for the routes of use question to capture environmental exposures, and both intentional and accidental misuse.
  - h. Replaced the optional frequency of use question with an optional lifetime exposure question
10. **Other Tobacco Products Used Section (TIR)** [See pp. 23-26 in TIR attachment]
- a. Section retitled to “Nonstudy Tobacco Products”
  - b. Minor rewording of instructions for clarity
  - c. Minor rewording of questions throughout this section for inclusiveness and logical reporting about either use or environmental tobacco exposures
  - d. Revised list of values for the tobacco product types and subtypes (same as in the Study tobacco products section)
  - e. New list of values for the frequency of product use question (same as in other sections)
11. **Additional Information Section** [See p. 26/28 in TPR attachment; p. 27/29 in TIR attachment]
- a. No changes
12. **Attachments Section** [See pp.27-28/28 in TPR attachment; pp. 28-29/29 in TIR attachment]
- a. Add two values for types of attachments relevant to researchers (TIR only): case report forms and documents from oversight bodies.
13. Technical, functionality or informational changes to improve the submitter experience in using the questionnaires
- a. All selectable items can now be unselected if the submitter makes a mistake or changes their mind during initial data entry.
  - b. The custom designed informational link showing images and text descriptors of tobacco products (previously posted to <https://www.safetyreporting.hhs.gov/srp2/CTP/TobaccoProductTypes.html> ) is retired and replaced by a link to a public webpage for a similar purpose (<https://www.fda.gov/tobacco-products/products-guidance-regulations/products-ingredients-components> ). The public webpage is designed, maintained, and routinely updated by experts in CTP’s Office of Health Communication and Education (OHCE).
  - c. Additional business rules catch more inconsistencies in responses – mocked up in various documents referenced herein.
14. **Mobile TPR (TPRM1)** [See Mobile attachment]
- a. The mobile version, as OMB-approved and developed (2020), was never released to the public due to technical and formatting issues. Development efforts continued, anticipating release with the rest of the package described herein (2021). The concept of the mobile RQ continues to be a shorter version of the TPR, available only to guest submitters who must include an image with their submission. As before, submitters using a mobile device (phone or tablet, not laptop) must choose if they wish to see the desktop or the mobile version of the questionnaire. Compared to the desktop, the mobile RQ contains two of four Report Information questions, most Contact Information questions (optional), all but three of the Problem Summary questions, roughly half of the Main Tobacco Product Details questions, all of the Tobacco Product Use or Exposure Details questions, none of the “Other Tobacco Products” questions, the one Additional



Information question, and the unique requirement to upload at least one attachment. The total number of required questions in the mobile view is the same as in the desktop, plus the one requirement for an attachment.

15. The **optional existing exit and submit surveys** are unchanged with 2 questions each. [See Evaluation attachment]

#### **Numbers of Required Questions within the Voluntary Reports to each RQ after incorporating the changes above:**

- Four questions continue to be required at the SRP level to navigate to the correct RQ out of the ~ 10 RQs hosted by FDA and NIH- this is outside of CTP's direct control.
- A tobacco-related health problem report can be submitted by answering as few as nine questions inside the TPR for most tobacco product types.
- A report of both a health and a product problem for the ENDS tobacco product type, can be submitted by answering as few as 13 questions inside the TPR.
- To submit a report to the TIR, eleven<sup>3</sup> research-specific questions are required (one is new) in addition to the 9 or 13 from the above TPR examples (for totals of 20 or 24).

#### **Resources:**

The live 2020 versions of both RQs (TPRv4 and TIRv3) can be accessed at <https://www.safetyreporting.hhs.gov> .

#### **References:**

IARC (2018). 3.1 Measuring tobacco use behaviors. Retrieved 10/19/2020 from [https://www.iarc.fr/wp-content/uploads/2018/07/Tobacco\\_vol12\\_3A.pdf](https://www.iarc.fr/wp-content/uploads/2018/07/Tobacco_vol12_3A.pdf)

Pearson, J. L., et al. (2018). "Recommended core items to assess e-cigarette use in population-based surveys." *Tobacco Control* 27(3): 341-346. <http://dx.doi.org/10.1136/tobaccocontrol-2016-053541> for CORE items in ENDS national surveys

J.O. Prochaska, C.C. DiClemente. (1983). Stages and processes of self-change of smoking: toward an integrative model of change. *J. Consult. Clin. Psychol.*, 51 pp. 390-395

Weaver, S. R., et al. (2018). "Establishing consensus on survey measures for electronic nicotine and non-nicotine delivery system use: Current challenges and considerations for researchers." *Addictive Behaviors*, 79: 203-212. <https://doi.org/10.1016/j.addbeh.2017.11.016>

UDSHHS/FDA/CTP. (2020, April). Enforcement Priorities for Electronic Nicotine Delivery Systems (ENDS) and Other Deemed Products on the Market Without Premarket Authorization (Revised): Guidance for Industry. Available from <https://www.fda.gov/media/133880/download> .

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<sup>3</sup> This count of 11 includes the two optional questions to be converted to required questions in a delayed manner (Principal Investigator Name and Clinical trial site).

USDHHS/NIH/National Institute on Drug Abuse. (2018, January). "Principles of Drug Addiction Treatment: A Research-Based Guide (Third Edition) - Types of Treatment Programs." Retrieved October 15, 2020, from <https://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/drug-addiction-treatment-in-united-states/types-treatment-programs> .