COLLEGE of AMERICAN PATHOLOGISTS

Laboratory Quality Solutions

# Customization of the CAP Lung Cancer Biomarker Reporting Template to Facilitate Direct Population of Genomic Test Results by Molecular Laboratories

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## Introduction:

- Biomarker reporting has increasingly become a key component of pathology reporting, providing diagnostic, prognostic, and actionable therapeutic data for patient care, with laboratories worldwide relying on the College of American Pathologists (CAP) Cancer Protocols which are templates that provide guidelines for collecting the essential data elements for malignant tumors.
- Most cancer biomarker testing is currently carried out at a third-party reference laboratory with results being provided in a PDF format, thus making their incorporation into structured reports dependent upon manual solutions that are error-prone, time-consuming, not scalable, and typically not remunerated.
- The growth in biomarker testing for diagnosis, along with the increase in the number of biomarkers tested, has pushed for the development of mapping logic that allows for the seamless electronic auto-population of reference laboratory cancer biomarker test results into a structured data capture format.
- We have recently demonstrated the ability to auto-populate biomarker genomic test results with high fidelity from Caris Life Sciences into the CAP Lung Biomarker Protocol powered by mTuitive Pathology.
- Our initial study identified gaps in the ability of our template to capture all variants of genomic mutations which Caris reports as discrete data elements.
- Moreover, cases may arise where additional unusual mutations or variants of unknown significance (VUS) may impact patient care and therefore should also be included in the synoptic report.
- We describe here an approach for revising the CAP Lung Biomarker Reporting Protocol to capture all variants in a discretized format, as well as an approach for including additional fields for reporting VUS or other unexpected mutations.

## Methods:

- The CAP Lung Biomarker Protocols are modeled to capture the data elements in a structured report using the CAP-developed Single Source Product (SSP) software to assign metadata to question and answer sets, including unique identifiers (Ckeys), to each of the data elements.
- Molecular test results are delivered electronically by Caris Life Sciences as a JSON data-interchange file to the mTuitive Results Web Service.
- The JSON files containing sample data are then parsed by mTuitive to all possible question and answer sets contained in the CAP Lung Biomarker Protocol and matched to unique identifiers (cKeys) for the variants detected (Figure 1).
- The mTuitive algorithm maintains a map of cKeys for the section (parent to question), question, and answer.
- Caris data elements included in the mTuitive SQL parsing algorithm are shown in Table 1.
- The mTuitive software then generates the final synoptic report of the biomarker results.
- The high-level overview of the implementation of the process in a clinical setting is shown in Figure 2.


Figure 1: Sample PDF report of test results from Caris (left), JSON data transmission feed of an EGFR Exon 20 variant (middle), and the CAP Lung EGFR biomarker reporting elements with cKeys (right) used to direct data generated by the mapping and parsing software tool developed by mTuitive.

## Methods:

- **GenomicAlteration**
  - Biomarker Name
  - Result
  - hgvsProteinChange
  - Exon
- **CopyNumberAlteration**
  - Biomarker Name
  - Result
  - Copy Number (if available)
- **TumorMutationBurden**
  - Biomarker Name
  - mutation Burden Call
  - mutation Burden Score
- **MicrosatelliteInstability**
  - msiCall
- **Translocation**
  - Biomarker Name
  - Result
  - FusionISOForm
  - Gene1 & Gene2
- **Test Name - ALK, ROS1, HER2, NTRK1/2/3 & PD-L1**
  - Platform Technology
  - ExpressionAlteration
  - Results
- **Test Name - Mismatch Repair Status**
  - Test Results
    - Expression Alteration
      - Result
      - Gene[]

Table 1: JSON Data Elements reported by Caris that are included in mTuitive's SQL parsing algorithm.

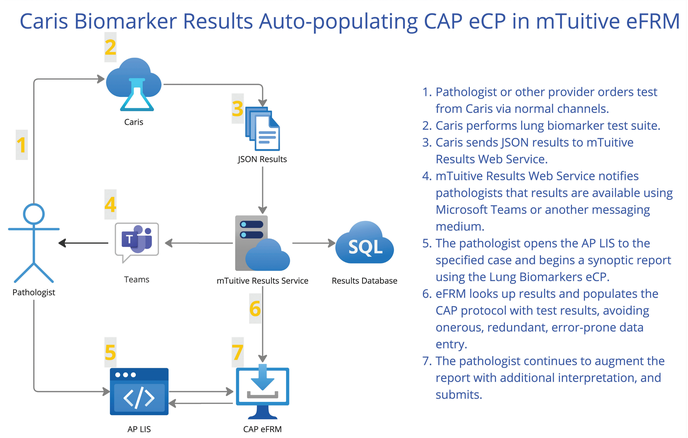
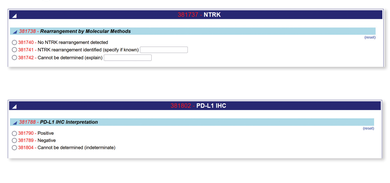



Figure 2: Clinical Workflow-for auto-population of Caris Biomarker results into CAP synoptic reports.

## Results:

- The CAP Lung Biomarker Protocol was expanded to include the capture of all fusion variants, such as NTRK and PD-L1, and record all the variants as discrete data; Figure 3 compares the original and modified Lung Biomarker Protocols.
- Figures 4 and 5 show the delineated JSON file that provides data on a broader range of variants reported by Caris for NTRK and PD-L1.
- Figure 6 shows elements that were added to the CAP Lung Biomarker Protocol to capture mutations of potential pathologic relevance and VUS not usually applicable to non-small cell lung cancer but that might be of concern to patients.

### Original Protocol




### Modified Protocol

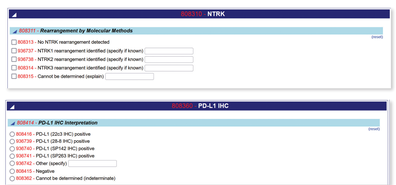



Figure 3: Comparison of structured data capture for the CAP Lung Biomarker Protocol between the original protocol and the modified protocol which contains expanded pick lists for NTRK and PD-L1 variants reported by Caris.

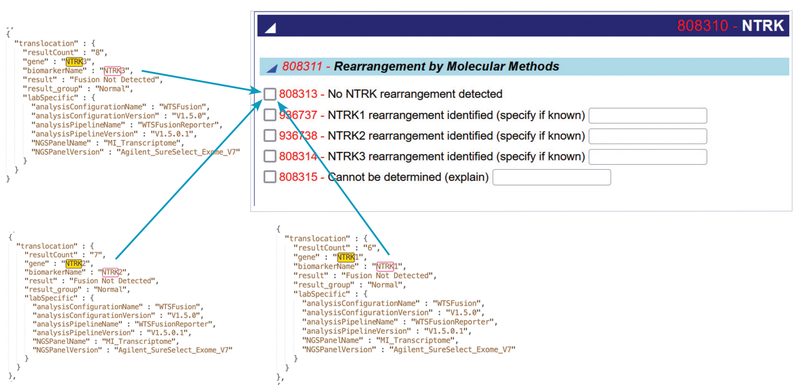



Figure 4: Mapping of JSON NTRK results to their corresponding elements (with unique cKeys) in the CAP protocol. In these examples, rearrangements of NTRK1 (936737), NTRK2 (936738), and NTRK3 (808314) were not identified so these negative results would be mapped to result element 808313 (No NTRK rearrangement detected) in the CAP protocol.

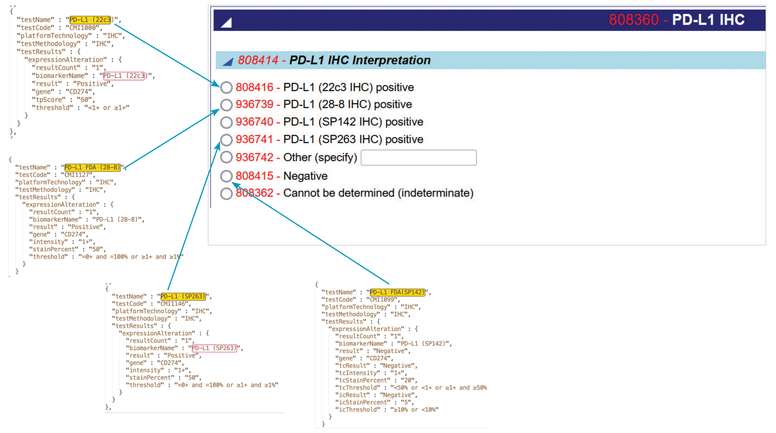
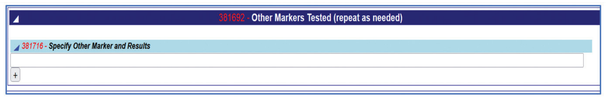



Figure 5: Mapping of JSON PD-L1 results to their corresponding elements (with unique cKeys) in the CAP template. In cases where PD-L1 (22c3), PD-L1 (28-8), and PD-L1 (SP263) would be identified, they would be mapped to result elements 808416, 936739, and 936741, respectively, in the CAP Template. PD-L1 (SP142) was not identified in the example shown and would be mapped to result element 808415 (Negative).

### Original Protocol




### Modified Protocol

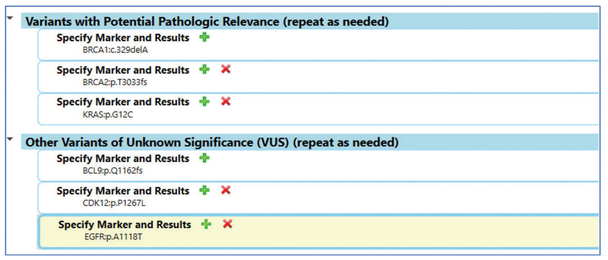



Figure 6: Modified design of the Original Template to allow for the capture of additional variants with potential pathologic relevance or unknown significance that are reported by Caris but would not have been highlighted in the CAP Lung Biomarker Template.

## Conclusions

- Biomarker reporting has increasingly become a key component of pathology reporting, providing diagnostic, The ability of molecular testing laboratories to directly populate genomic test results into CAP Biomarker Reporting Protocols is a significant technological advance.
- Direct population of results eliminates the need for further manual manipulation by the pathologist to search and enter relevant findings from a multipage PDF document into a more concise synoptic report.
- While the current CAP Biomarker Protocols set the standard for reporting relevant genomic information in each tumor type, it is likely that further adaptations of these protocols, as well as further refinement of data reporting and parsing, will be needed for flexibility in meeting the needs of different molecular laboratories and laboratory information systems.
- Plans are in development to design a pilot study to examine this on a larger scale in a clinical setting.

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