FRPath.org Country and FRP Information Input Form		
Country: United States of America	**Agency Name:** United States Food and Drug Administration (USFDA)	
Name of FRP: FDA Real Time Oncology Review-RTOR		
Is this FRP Proposed or Active? Active		
Date FRP was officially enacted: Click here to enter a date.		
1. Facilitates activities during development	**2. Accelerates the regulatory review process**	**3. Relies on or recognizes a prior regulatory decision**
☒	☒	☐

Is a Guidance or SOP describing how to apply this FRP publicly available?	Yes- see reference below
When should the FRP be requested?	Before the marketing authorisation submission
Does the agency provide assistance/advice to the sponsor?	Yes- For any product type
For which types of product(s) can this FRP be used? E.g. NMEs, generics, biologics, biosimilars, all products	For the pilot program, New Drug Application (NDA) and Biologics License Application (BLA) submissions will be selected from each clinical division (DO1, DO2, DO3 and DHM1 and DHM2) to evaluate the feasibility and to optimize the process for RTOR. Acceptance into the RTOR pilot does not guarantee or influence approvability of the application, which is subject to the usual benefit-risk evaluation by FDA reviewers. Participation by the applicant in this pilot program is voluntary. The following criteria are used for a supplemental new drug application to be selected for RTOR: - Drugs likely to demonstrate substantial improvements over available therapy, which may include drugs previously granted Breakthrough Therapy Designation for the same or other indications. Drugs meeting other criteria for other expedited programs (e.g. fast track, priority review) may also be considered. - Straight forward study designs, as determined by the review division and the OCE. Studies conducted exclusively outside the U.S. and adjuvant, neoadjuvant, and prevention studies will be excluded. - Endpoints that can be easily interpreted (for example, overall survival in a randomized trial). - Supplements with chemistry, manufacturing and control formulation changes and supplements with pharmacology/ toxicology data will be excluded. - Submissions with greater complexity, including

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	those with companion diagnostics, may also be excluded for the purposes of the pilot program.
Must the product address an unmet medical need or serious condition?	Negotiable
If a fee is required, what is the amount (in US$ equivalent)	For supplemental applications, no fees are necessary. For new molecular entities, PDUFA fees (when applicable) will be due when the first component of the RTOR is submitted.
Total target (agency) time for assessment (calendar days)	**Standard Operating Procedures** *Please note that these milestones are provisional and may vary substantially across applications. The review team is expected to look at the presubmission materials when they are submitted and to discuss their findings with the CDTL and Division Director.* - Week 0-3: At the time of top-line results of a pivotal trial, if the eligibility criteria above is met, an applicant can apply for the RTOR pilot by submitting a request via email to the appropriate application RPM. The clinical division director/deputy director, the review team (including reviewers, team leaders, and management from all relevant review disciplines, and CDRH as applicable) and OCE management will jointly decide whether the application can be selected for the RTOR pilot program. This decision will generally be made in approximately 15 business days of the receipt of notification through the appropriate division RPM. - Week 3-6: Once an application is selected, a teleconference with the applicant will be arranged in approximately 15 business days. The clinical division director/deputy director, the review team, and OCE staff will participate in this meeting. If the drug product is co-developed with a companion diagnostic, the diagnostic partner and CDRH should also be on the teleconference. If the applicant or the Agency determines that RTOR is not appropriate, a routine review procedure will be followed. Otherwise, FDA and the applicant will discuss the plan for RTOR in detail, reach tentative agreement on responsibilities, and proposed pre-submission timelines. The final SAP/protocol should be submitted as soon as possible. If the drug product is co-developed with a companion diagnostic, the applicant should outline timelines with the diagnostic partner and with CDRH. - Week 6-9: Under the RTOR program, the applicant would officially submit the following items to their marketing application as a pre-submission as soon as

they become available:

1. User fee, if applicable
2. Complete SDTM dataset package
3. Top line efficacy/safety tables/figures
4. Complete ADaM datasets for key efficacy and safety tables/figures for pivotal study (see OOD data specifications for requested format of safety datasets)
5. Key results, analysis, and datasets for other disciplines, if applicable.
6. Final study reports of all pharmacology and toxicology studies
7. Summary of data supporting dose and dosing regimen selection
8. The protocol and amendments (a list of major changes for each amendment), SAP, and DMC charter and DMC minutes
9. SAS programs
10. Proposed labeling
11. CRFs as required by regulation
12. All CMC information including list of all manufacturing, testing and critical intermediate facilities with addresses and FEI numbers other than stability data for registration batches (if not available) for drug substance(s), drug product.
13. Completed AAid.

- Week 10-16: Pre-submission meeting: In addition to responding to the applicant's questions in the meeting package, FDA may share with the applicant preliminary key review questions or issues and critical analyses needed. If FDA requests additional analyses, the applicant may submit them before or at the time of submission of the marketing application. In some cases, the applicant may submit the requested additional analyses after the marketing application is submitted. These discussions may be documented in the meeting minutes under the section, "Agreement of a Complete Application" for NMEs or original BLAs, under a new "Additional Items discussed" which can be added by the RPM for other applications or under specific questions as appropriate.
- Week 16-22: The applicant submits the complete marketing application. Once FDA receives the completed application, the review clock will start. The complete application will include any remaining

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	components previously not submitted in the presubmission.	
Total target (company) time for responses to agency questions (If stated)	See Section above.	
Select one of the following (* see definitions at end of document)		
Is this a verification review (a recognition pathway)?*	**Is this an abridged* review (selected dossier portions)? (a reliance pathway)?***	**Is this a full* review of all parts of the dossier?**
☐	☐	☒
If this is a reliance or recognition pathway, what are the accepted reference agencies?	No, this is not a reliance or recognition pathway.	
How many reference agency decisions are required?	Not applicable.	
Does this FRP require submission of Assessment Reports from prior decisions?	Not applicable	
Is a CPP (Certificate of Pharmaceutical Product) required for approval?	Not applicable	
Can an alternate form of reference documentation to the CPP be used? If so, what types of documents?	Not applicable.	
If this process is through a Regional Regulatory Initiative, which countries participate in this process?	No, this process is not through a Regional Regulatory Initiative.	
Does the product have to have been marketed in another country? For a specific amount of time? If so, for how long?	Not applicable.	
How are queries to the companies sent?	Choose an item.	
Are external reviewers (e.g. non-agency) involved in the assessment?	Choose an item.	
Post-authorization study commitments	Always required	
For how long is the initial approval or designation valid?	Choose an item.	
Any other details you wish to provide?	- The Oncology Center of Excellence Real-Time Oncology Review (RTOR) pilot program aims to explore a more efficient review process to ensure that safe and effective treatments are available to patients as early as possible, while maintaining and improving review quality and balancing the review team's workload through data and analysis	

	standardization, and early iterative engagement with the applicant. - The RTOR focuses on early submission of data that are the most relevant to assessing the product's safety and effectiveness. RTOR allows the FDA to review much of the data earlier, after the clinical trial results become available and the database is locked, before the information is formally submitted to the FDA. - The standard review time goal for drug applications is six or ten months, as outlined by the Prescription Drug User Fee act (PDUFA) VI Reauthorization Letter. In contrast, this pilot program aims to approve supplements much sooner. The goal is to increase the efficiency of the development and review of cancer drugs and improve FDA's rigorous standard for evaluating efficacy and safety by enhancing the process for evaluating the data submitted to the FDA.
Date of this update	13 APRIL 2020
References	1. "Real-Time Review of Drug Applications is Now a Reality" September 20, 2018 Issue. https://www.fda.gov/drugs/real-time-review-drug-applications-now-reality-september-20-2018-issue Accessed on 13 April 2020. 2. Real-Time Oncology Review Pilot Program. https://www.fda.gov/about-fda/oncology-center-excellence/real-time-oncology-review-pilot-program Accessed on 13 April 2020.

*Definitions:

Verification review: A checklist review based on recognition of a prior regulatory decision. Recognition is the routine acceptance of the regulatory decision of another regulator or other trusted institution. Recognition indicates that evidence of conformity with the regulatory requirements of economy A is sufficient to meet the regulatory requirements of economy B.

Abridged review: An abbreviated review of selected portions of the dossier and the reliance on prior assessment decisions. Reliance is the act whereby a regulatory authority in one jurisdiction may take into account/give significant weight to work performed by another regulator or other trusted institution in reaching its own decision

Full review: A comprehensive review of all components of the dossier. This may or may not be CPP-dependent. This may form part of a reliance or recognition pathway.

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