FRPath.org Country and FRP Information Input Form		
Country: Europe	**Agency Name:** European Medicines Agency (EMA)	
Name of FRP: EMA Marketing Authorisation under Exceptional Circumstances		
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	The legal basis for the marketing authorisation (MA) under exceptional circumstances is the Article 14 (8) of the Regulation (EC) No 726/2004, and the relevant documentation for applications in exceptional circumstances are laid down in Part II of Annex I of Directive 2001/83/EC, as amended. Products for which the applicant can demonstrate in this application that he is unable to provide comprehensive data on the efficacy and safety under normal conditions of use, because: (i) the indications for which the product in question is intended are encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, or (ii) in the present state of scientific knowledge, comprehensive information cannot be provided, or (iii) it would be contrary to generally accepted principles of medical ethics to collect such information, may be eligible for marketing authorisation under exceptional circumstances. Consequently, the authorisation under exceptional circumstances is granted subject to a requirement for the applicant to introduce specific procedures, in particular concerning the safety of the medicinal product, notification to the competent authorities of any incident relating to its use, and action to be taken. A marketing authorisation under exceptional circumstances should not be granted when a conditional marketing authorisation is more appropriate. A conditional marketing authorisation is for example granted in the absence of comprehensive clinical data when it is likely that the applicant will be in the position to provide such data in a

	short timeframe, whereas the fulfilment of any specific procedures/obligations imposed as part of the marketing authorisation under exceptional circumstances is aimed at the provision of information on the safe and effective use of the product and will normally not lead to the completion of a full dossier. **PARTICULARITIES OF THE MARKETING AUTHORISATION UNDER EXCEPTIONAL CIRCUMSTANCES:** (i) It should be noted that designated orphan products are eligible for approval under exceptional circumstances only if the criteria considered for the approval under exceptional circumstances are fulfilled; (ii) The summary of product characteristics and package leaflet should mention that a marketing authorisation has been granted subject to certain specific obligations to be reviewed annually; (iii) The renewal of the marketing authorisation of a medicinal product under exceptional circumstances follows the same rules as a "normal" marketing authorisation. After 5 years, the marketing authorisation will then be renewed under exceptional circumstances for an unlimited period, unless European Medicines Agency pre-authorisation procedural advice for users of the centralised procedure EMA/339324/2007 Page 30/133 the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. (See the renewal guidance).
Must the product address an unmet medical need or serious condition?	Yes
If a fee is required, what is the amount (in US$ equivalent)	Marketing-authorisation application (single strength, one pharmaceutical form, one presentation): From €296,500. Fee reductions and incentives are available for micro, small and medium-sized enterprises (SMEs), designated orphan medicines, multiple applications on usage patent grounds and other classes of application. Full details on all fees and fee reductions are available in the explanatory note: https://www.ema.europa.eu/documents/regulatory-procedural-guideline/explanatory-note-general-fees-payable-european-medicines-agency-1-april-2020_en.pdf
Total target (agency) time for assessment (calendar days)	Click here to enter text.
Total target (company) time for responses to agency questions (If stated)	Click here to enter text.

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)?**	**Is this a full* review of all parts of the dossier?**

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	(a reliance pathway)?*	
☐	☐	☒

If this is a reliance or recognition pathway, what are the accepted reference agencies?	No, this process 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?	Member States of the European Union (EU) and the European Economic Area (EEA).
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?	Yes- as needed
Post-authorization study commitments	Always required
For how long is the initial approval or designation valid?	4-5 years
Any other details you wish to provide?	- As early as possible during drug development, the applicant is encouraged to seek scientific advice from the EMA about the justification for applying for a marketing authorisation under exceptional circumstances, especially on the inability to provide comprehensive data. Any further discussion on the appropriateness should preferably occur in the context of the pre-submission meeting. - TIMING OF THE SUBMISSION AND DOCUMENTATION TO BE SUPPLIED: First of all, the applicant should submit a statement on the appropriateness of the granting of a marketing authorisation under exceptional circumstances in the notification to the EMA of their intention to submit a marketing authorization application (at least 6 months before submission). Then, if the

	applicant considers that the grounds for approval under exceptional circumstances should apply, the applicant should tick the box 1.5.2 of the application form and include its justification in module 1, covering the following aspects: (1) A claim that the applicant can show that he is unable to provide comprehensive non-clinical or clinical data on the efficacy and safety under normal conditions of use; (2) A listing of the non-clinical or clinical efficacy or safety data that cannot be comprehensively provided; (3) Justifications on the grounds for approval under exceptional circumstances. European Medicines Agency pre-authorisation procedural advice for users of the centralised procedure EMA/339324/2007 Page 29/133; (4) Proposals for detailed information on the specific procedures/obligations to be conducted (Safety procedures, programme of studies, prescription or administration conditions, product information). The proposals for detailed information on the specific procedures/obligations to be conducted shall also be written in accordance with the "Guideline on risk management systems for medicinal products for human use". - The Rapporteur, Co-Rapporteur and the other CHMP members will assess the justification/data submitted for exceptional circumstances as part of the overall assessment of the benefit/risk of the application. It is up to the CHMP, during the review, to ultimately decide on the type of the marketing authorisation.
Date of this update	30 May 2020
References	1. Fees payable to the European Medicines Agency. https://www.ema.europa.eu/en/human-regulatory/overview/fees-payable-european-medicines-agency Accessed on 30 May 2020. 2. Pre-authorisation guidance. https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/pre-authorisation-guidance Accessed on 30 May 2020. 3. GUIDELINE ON PROCEDURES FOR THE GRANTING OF A MARKETING AUTHORISATION UNDER EXCEPTIONAL CIRCUMSTANCES, PURSUANT TO ARTICLE 14 (8) OF REGULATION (EC) NO 726/2004. https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guideline-procedures-

granting-marketing-authorisation-under-exceptional-circumstances-pursuant/2004_en.pdf Accessed on 30 May 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.