Regional Comparisons of Expedited Pathways in US, EU and China

parexel BIOTECH

Conditional Approval Pathway Comparison

	US	EU	CHN
Name	Accelerated Approval	Conditional Marketing Authorization	Conditional Approval
Issued year	1992	2006	Formally issued in July 2020, while there were actual practice before.
Agency for designation	FDA	EMA	NMPA CDE

Eligibility criteria	• A drug that treats a serious condition **AND** generally provides a meaningful advantage over available therapies **AND** demonstrates an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality (IMM) that is reasonably likely to predict an effect on IMM or other clinical benefit (i.e., an intermediate clinical endpoint)	• Granted to a medicinal product that fulfils an unmet medical need when the benefits to public health of immediate availability outweighs the risk inherent in the fact that additional data are still required.
		• CMA is a "temporary authorization" based on "less complete data than is normally the case and subject to specific obligations."
		  • Surrogate endpoints
		  • Incomplete data in some respect
			• Products for seriously life-threatening disease without effective treatments, **OR** for urgent needs in public health, and the efficacy has been verified, the clinical value could be predicted;
			• Vaccines for major public health emergencies or other vaccines that are urgently needed as identified by the National Health Commission, if benefits outweigh risks

When to submit request	During development	To discuss the development plans with the EMA early in the development process; submit conditional marketing authorization (CMA) request 6-7 months before MAA submission; If applicants submit CMA with the MAA, the CHMP can issue its comments during MAA review.	During development and MAA stage
Timelines for response	Not specified	Not specified	Not specified
Advantage	• Approval based on an effect on a surrogate endpoint or an intermediate clinical endpoint that is reasonably likely to predict the drug's clinical benefit.	• To get earlier marketing approval based on less comprehensive clinical data.	• Approval based on an effect on a surrogate endpoint or an intermediate clinical endpoint that is reasonably likely to predict the drug's clinical benefit. • Ph3 IA of public emergency vaccine.
Termination	If PAC meet the requirements.	A CMA reverts to full authorization on completion of specific obligations by MAH as agreed with EMA	If PAC meet the requirements, transfer to regular approval. Or else, terminate.

parexel BIOTECH

Priority Review Pathway Comparison

	US	EU	CHN
Name	Priority Review	Accelerated Assessment	Priority Review
Issued year	Prescription Drug User Fee Act of 1992	Article 14(9) of Regulation EC No 726 / 2004	Formally issued in July 2020. Involved in related regulations from 2015.
Agency for designation	FDA	EMA	NMPA CDE
Eligibility criteria	• Drugs applying for original BLA/NDA or efficacy supplement for serious diseases, if approved, can improve safety or effectiveness significantly; • **OR** any supplement intend to change labels based on pediatric study report under 505(A); • **OR** a drug intended for a specific infectious disease; • **OR** awarded with the Priority Review Voucher	• For medicinal products that are of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. As for PRIME	• Shortage products with urgent medical needs, innovative and modified innovative drugs for the prevention and treatment of major infectious diseases or rare diseases • Innovative products, new dosage forms and new strengths of pediatric drugs • Urgent needs Vaccines and innovative vaccines • Products included into the BTD • Products included into the conditional approval • Other circumstances by NMPA
When to submit request	With original BLA, NDA or efficacy supplement	An EMA pre-submission meeting request 6-7 months before MAA submission is advised and to discuss the plan for AA. Submit AA request 2-3 months before MAA submission. If the drug already included in the PRIME program, applicant would receive confirmation that their medicine might potentially be eligible for accelerated assessment.	At MAA stage
Timelines for response	Response within 60 days of the receipt of original BLA, NDA or efficacy supplement.	The CHMP conclusions will be communicated to the applicant when CHMP meeting completed.	Pre-NDA Meeting response (60 WDs), PR request (5+5 WDs).
Advantage	• Shortened review time for listing application (6 months under priority review VS 10 months under standard review)	• Shortened review time (from the standard review of 210 days to 150 days)	• Shortened review time (from standard 200 WDs to 130 WDs / 70 WDs) • Other related processes can also be prioritized.
Termination	If filing gets a complete response letter due to deficiencies in the application it goes off the review clock	Revert to standard assessment time if Major objections identified	If the filing dossier can't meet the conditions of Priority review during MAA review period

parexel BIOTECH

Breakthrough Therapy Designation Comparison

	US	EU	CHN
Name	Breakthrough therapy designation	PRIME (Priority Medicine)	Breakthrough therapy drug procedure
Issued year	2012	2016	2020
Agency for designation	FDA	EMA	NMPA CDE
Eligibility criteria	• A drug that is intended to treat a serious condition **AND** preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on a clinically significant endpoint(s) over available therapies.	• For medicinal products of major public health interest and in particular from the viewpoint of therapeutic innovation. • Target conditions where there is an unmet medical need with the potential to address the unmet medical need and the potential to bring a major therapeutic advantage.	Innovative drugs or modified new drugs, which are: • Intended for the prevention and treatment of serious life-threatening diseases, or diseases that seriously affect the quality of life, **AND** • Have no effective ways of prevention and treatment, **OR** for which sufficient evidence is available to demonstrate they are significantly clinically superior over existing available treatments
When to submit request	With IND or after; ideally, before the phase III clinical trial.	Preliminary clinical evidence in patients to demonstrate proof of concept. In exceptional cases can be with FIH data and compelling nonclinical data in a relevant model	In the stage of phase I / II clinical trial. Usually, no later than the start of phase III clinical trial.
Timelines for response	Within 60 calendar days of receipt of the request	Generally, within 40 days of the start of the procedure.	Within 45 WDs of the receipt of the application
Advantage	• Intensive guidance on efficient drug development • Organizational commitment • Other actions to expedite review	• Early appointment of Rapporteur • Kick-off meetings • dedicated EMA contact point • scientific advice • Confirmation of potential for accelerated assessment at MAA	• Prioritized resources for communication and intensive guidance on efficient drug development • Type I meeting opportunity • Potential priority review for NDA
Termination	Designation may be rescinded if it no longer meets the eligibility criteria for BTD.	PRIME support may be withdrawn if emerging data were to show that the criteria are no longer met. However, this should not impact on the eligibility of the product to the centralized procedure	Designation may be rescinded if it no longer meets the eligibility criteria for BTD.

BTD: http://www.fda.gov/forpatients/approvals/fast/default.htm
PRIME: https://www.ema.europa.eu/en/human-regulatory/research-development/prime-priority-medicines
SAKIGAKE Designation System: https://www.mhlw.go.jp/english/policy/health-medical/pharmaceuticals/170421-01.html &https://www.pmda.go.jp/english/review-services/reviews/advanced-efforts/0001.html

parexel BIOTECH

Orphan Drug Designation Comparison

	US	EU	CHN
Name	Orphan Drug Designation	Orphan Drug Designation	**NO ODD in China**
Issued year	Orphan Drug Act in1983	Regulation (EC) No 141/2000	N/A
Agency for designation	FDA	EMA	NMPA CDE
Eligibility criteria	• Treat, prevent, or diagnose a rare disease • Involve a condition with a prevalence not over 200,000 people in the USA	• Treat, prevent, or diagnose a life-threatening or chronically debilitating disease • Involve a condition with a prevalence not over 5 in 10,000 in EU, or be unlikely to generate sufficient returns to justify the investment necessary for development • Involve a condition for which no satisfactory method of diagnosis/prevention/treatment is authorized or, if such a method exists, the medicine must be of significant benefit to those affected	• Products target the disease in national 121 rare disease list are eligible for priority review procedure • 41 rare disease drugs in urgent medical needs drug lists (3 batches) may apply MAA and priority review directly based on foreign data, **the MAA review duration is 70WDs**. In general, Post marketing commitment (PMC) is needed.
When to submit request	Preclinical or clinical data stage At least relevant *in vitro* and *in vivo* data in appropriate preclinical models should be submitted.	Preclinical or clinical data stage. At least relevant *in vitro* and *in vivo* data in appropriate preclinical models should be submitted.	Follow priority review procedure
Timelines for response	Typically 60-90 days but may be longer based on work load and staffing	Within 90 days of start of procedure (fixed timetable)	N/A
Advantage	• Tax credits for qualified clinical trials • Exemption from user fees • Potential seven years of market exclusivity after approval	• 10 years of market exclusivity (10 years protection from market competition with similar medicines with similar indications) • Administrative/procedural assistance for SMEs • Fee reductions • Incentives	• Shorten review duration (130/70WDs compared to standard 200WDs) • Less/no Chinese data needed to support MAA
Termination	Sponsor can withdraw	Maintenance of OD status is reviewed at time of MAA and may be withdrawn. MAH may voluntarily remove OD status.	N/A

parexel BIOTECH