Regulatory Filing Pathways in The European Union for Drug Products

Gita Rao

Aurobindo Pharma Limited

Countries of EU covered by these pathways

Austria (AT)	Belgium(BE)	Bulgaria(BG)
Croatia(HR)	Cyprus(CY)	Czech Republic(CZ)
Denmark(DK)#	Estonia(EE)@	Finland(FI)#
France(FR)	Germany(DE)	Greece(EL)
Hungary(HU)	Ireland(IE)	Iceland(IS)*
Italy(IT)	Latvia(LV)@	Liechtenstein(LI)*
Lithuania(LT)@	Luxembourg(LU)	Malta(MT)
Netherland(NL)	Norway(NO)*#	Poland(PL)
Portugal(PT)	Romania(RO)	Slovakia(SK)
Slovenia(SL)	Spain(ES)	Sweden(SE)#

*The European Economic Area(EEA)

Nordic countries

@ Baltics

Regulatory pathways for filing

1.National procedure

2. Mutual recognition procedure

3.Decentralized procedure

4. Centralized procedure

Common to all procedures is Validation phase & Assessment phase. For all procedures except for National procedure, there is National phase where translations into local language are finalized

National procedure

Filing with regulatory authority of one country

Some indicative fees:

Country	First strength		Each subsequent strength	
	In Euros	*In INR*	*In Euros*	*In INR*
Germany	28200	22,62,768	6000	480,000
France	14700	11,76,000	14700	11,76,000
Netherlands	28730	22,98,400	NA	NA
Spain	8776.68	7,02,134	8776.68	7,02,134
Portugal	1759.56	1,40,764	291.56	23,324

National procedure (contd.)

Advantage:

Regulatory filing fee is lower than that of other procedures

Disadvantages:

-Barring Portugal(6 months-1 year), approval time is uncertain and long (3-5 years)

-While the National procedure is on-going, the Applicant or any of its related company/ies, cannot file dossier for same product in any other country of EU

Mutual Recognition procedure (MRP)

If nationally approved MA available in any one country of EU, this can be mutually recognized in any other country/ies using this procedure

The country where the national Marketing Authorization (MA) is approved is designated as the “Reference member state” (RMS) if it accepts to run the MRP on the request of the Applicant

The RMS needs to write an assessment report and circulate the same to all member states which are to be part of the MRP i.e. to the “Concerned member states” (CMS)

Following successful validation, the procedure will be closed in 90 days if there is consensus. National phase will follow.

Mutual Recognition procedure (MRP) (contd.)

Some indicative fees:

Country	RMS				CMS			
	First strength		Each subsequent strength		First strength		Each subsequent strength	
	In Euro	In INR	In Euro	In INR	In Euro	In INR	In Euro	In INR
Malta	10000	8,00,000	2000	1,60,000	250	20,000	250	20,000
Portugal	5115	4,09,200	1314.56	1,05244	3069	2,45,520	613.80	49,104
Netherlands	17210	13,76,800	NA	NA	9580	7,66,400	NA	NA

Mutual Recognition procedure (MRP) (contd.)

Advantages:

The timeline of this procedure itself is maximum 90 days

It is possible to withdraw MA from a country if sales are low

Disadvantages:

-National approval should not be very old (>3years) otherwise it takes too long for assessment report compilation

-Not all countries agree to conduct MRP

Decentralized procedure (DCP)

If Applicant wants to get Marketing authorizations in more than one EU countries at one go, this procedure is used. The chronological steps are as follows:

-One of the EU country is requested to accept the responsibility for conducting the procedure for the Applicant –being the “Reference member state” (RMS). Higher fees are paid to the RMS.

-A date for submission of the dossier to all the member states in the DCP is agreed between the Applicant and the RMS

-On the designated date, the Applicant submits the dossier to the RMS & all the CMSs in the procedure

-Following successful validation, the RMS circulates the DCP calendar

-On Day 70, the RMS circulates the detailed assessment report along with list of questions

-On Day 100, t

he CMSs circulate additional questions, if any

-At Day 105, the procedure is stopped and the Applicant has 3 months to submit the draft responses to the RMS

-If the RMS finds the draft responses grossly acceptable, it issues time-table for the second phase of the DCP. The Applicant circulates the final Day 106 response to all member states

-At Day 120, the RMS circulates yet another assessment report and list of questions

-At Day 145, the CMSs circulate additional questions, if any

-At Day 160, the Applicant circulates response to all member states

-At Day 180 the RMS circulates yet another assessment report and list of questions, if any

-At Day 195, the CMSs circulate additional questions, if any

-The Applicant sends responses as fast as possible. Any outstanding questions here after are quickly posed and responded till at Day 210 the procedure is closed

-National phase follows

Decentralized procedure (DCP)(contd.)

Some indicative fees:

Country	RMS				CMS			
	First strength		Each subsequent strength		First strength		Each subsequent strength	
	In Euro	In INR	In Euro	In INR	In Euro	In INR	In Euro	In INR
Malta	23000	18,40,000	2000	1,60,000	250	20,000	250	20,000
Portugal	7672.50	6,13,800	1759.56	1,40,760	3069	2,45,520	613.80	49,104
Netherlands	45940	36,75,200	NA	NA	22960	18,36,800	NA	NA

Decentralized procedure (DCP)(contd.)

Advantages:

Technical assessment of the dossier gets completed in more than one member state within a year

We can choose the member states we want to operate in and hence keep the filing fee lower

It is possible to withdraw MA from a country if sales are low

Disadvantages:

Very difficult to get DCP appointment when the dossier is ready…atleast 6-12 months advance booking is required

Centralized procedure (CP)

If an Applicant wants to get Marketing authorizations in all 30 EU countries, **at one go**, this procedure is used.

This procedure is conducted by European Medicines Evaluation Agency (EMEA)

The Applicant needs to apply to EMEA to run a CP. EMEA will appoint a rapporteur and a co-rapporteur to conduct the procedure

The steps of the procedure are similar to those described in DCP

Timeline needed to complete the procedure is less than a year if everything goes well

Fees:

Single strength with one presentation: Euros 3,13,200 (INR 2,50,56,000)

For each additional strength with one presentation: Euro 31,500(INR 25,20,000)

For each additional presentation: Euro 7,800 (INR 6,24,000)

Centralized procedure (CP) (contd.)

Advantages:

In a single review, marketing authorization can be secured in all 30 countries of EU

Product to be supplied to all countries will be uniform which aids supply chain

Disadvantages:

Very expensive in terms of regulatory fees

Life cycle management costs very high

Applicant needs to continue maintaining MAs in all countries even if no sale is happening in them

Life Cycle Maintenance

Variations (administrative, quality & safety):

-Type 1a

-Type 1aIN

-Type 1b

-Type 2

PSUR: Periodic safety update reports

Renewal: After 5 years

Sunset clause

Some EU Specific Concepts and Activities

EU Qualified Person for Quality: EUQP

EU Qualified Person for Pharmacovigilance: EUQPPV

European Directorate for quality of Medicines and Health care: EDQM

EU GMP certification

Primary and secondary packing in EU

Batch testing in EU

Batch release in EU

Country release

THANK YOU