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SCIENCE MEDICINES HEALTH

PRIME: Implementation of new initiatives to further strengthen the PRIME scheme

10th Industry stakeholder platform on research and development support

Kevin Cunningham and Anna Gross 11 July 2023
EMA PRIME, Scientific Evidence Generation Department, EMA

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- Introduction – PRIME, 5 year analysis and recommendations
- Pre-submission support for Applicants
- Implementing recommendations – progressing new pilots
- Future of PRIME procedures and activities in IRIS

PRIME: inception, implementation, evolution

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Foster development of medicines with major public health interest

Reinforce scientific and regulatory advice

- Foster and facilitate early interaction
- Raise awareness of requirements earlier in development

Optimise development for robust data generation

- Focus on efficient development
- Promote generation of robust and high-quality data

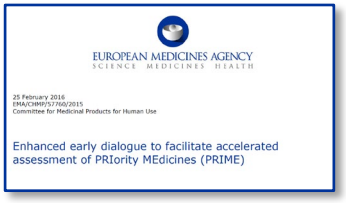
Enable accelerated assessment

- Promote generation of high quality data
- Facilitated by knowledge gained throughout development

2015

Draft reflection paper on Priority Medicines scheme

2016



2018

2021

2023

EMA launches features following 5Y analysis recommendations

PRIME: Analysis of the first 5 years' experience

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- 17 out of 19 PRIME products started under accelerated assessment.
- PRIME products are more complex (44% ATMPs, 94% orphans)
- PRIME products appear more likely to maintain accelerated assessment, despite higher complexity
- Reduction of clock stop for all category of products, most significantly for SME applicants.

Where PRIME is working

- Satisfaction with EMA and regulator's support
- High likelihood to use PRIME again
- Industry survey: Rapporteur appointment, EMA contact point

PRIME recommendations

- Allow more flexible, dynamic provision of SA
- Strengthen knowledge building to support AA
  - Product development tracker as basis for interactions
  - Submission readiness meeting to prepare for MAA
- Scope & timing of eligibility to PRIME

PRIME – Benefits and Enhanced Support

Benefit	Stage	Details
Appointment of PRIME Scientific Coordinator	**Immediately** after PRIME eligibility is granted	Dedicated EMA contact point to coordinate all support provided through PRIME
Early appointment of CHMP or CAT rapporteur	**One month** after PRIME eligibility is granted	Discussion on technical and scientific preparatory aspects of the marketing authorisation application
Kick-off meeting with rapporteur and multidisciplinary group of experts from EMA / European medicines regulatory network	**Three-four** months after PRIME eligibility is granted	Guidance on overall development plan, future scientific advice and regulatory strategy
Iterative scientific advice on overall development plans and key issues **NEW in 2023** Supported by Regulatory Roadmap and development tracker)	At any stage, and at major development milestones	Opportunity to involve other stakeholders such as health technology assessment (HTA) bodies, patients and the US Food and Drug Administration (FDA)
Expedited follow-up scientific advice (under certain criteria) with shortened timelines **NEW in 2023**	At any stage	Increased flexibility in providing scientific advice and a shortened timeline for related procedures
Submission readiness meeting **NEW in 2023**	Approximately one year ahead of marketing authorisation application	Discussion on development status and dossier maturity, application type (e.g. conditional marketing authorisation application), post-marketing evidence-generation and potential regulatory challenges
Confirmation of potential accelerated assessment	At time of marketing authorisation application	Increased certainty of assessment timelines

PRIME – Guidance and pre-submission support for Applicants

- Updated streamlined PRIME **guidance and webpage** launched March 2023
- PRIME Q&A for Applicants – single location for guidance for PRIME Eligibility Application and for PRIME designated products
- New from March 2023 EMA broadened pre-submission support to all applicants (now including non-SME/academia) planning a PRIME application, including the possibility of a virtual pre-submission meeting.
- Applicant submits a summary of the justification for PRIME eligibility (2-3 pages maximum) including:
    - Information on the product and its stage of development
    - An overview of the rationale on meeting the criteria for unmet medical need
    - High level summary of relevant clinical and non-clinical data to support the product's potential to address the unmet medical need.
- EMA PRIME team provide early feedback (written and/or TC) on approach and
- High uptake from Applicants in first 3 months since launch.

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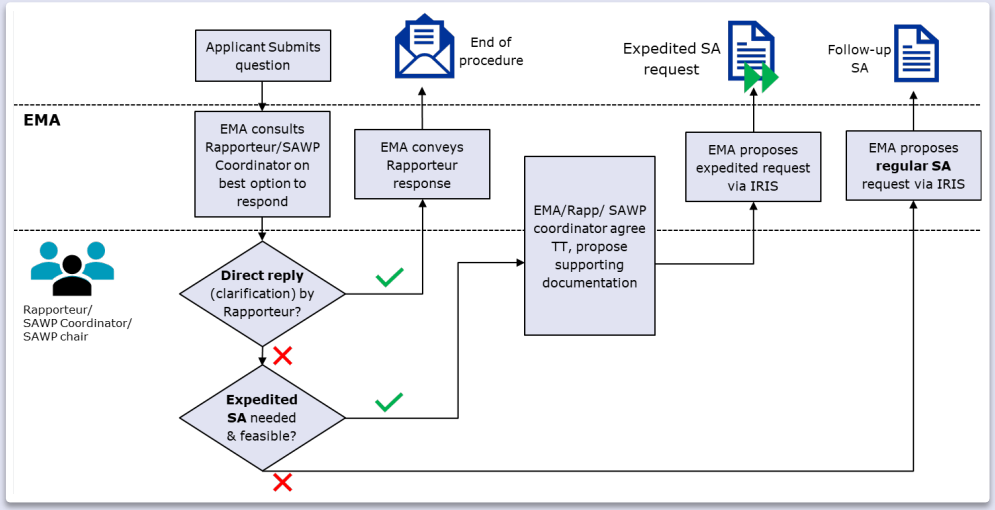
Flexibility of Scientific advice: New Expedited Procedure

- Transparent path for discussing and escalating issues arising during development
- Criteria for expedited advice:
  - Initial SA has already been sought on the overall development i.e. follow-up advice
  - Concerns issues with specific, well-defined scope (not limited to single discipline)
  - Advice is justifiably required more urgently than the standard SA timeline allows
- Streamlined submission process and dossier
- Reduced timeline (4-6w Vs 11-12w)



Aim: A dynamic, rapid procedure to deliver formal CHMP advice on issues impacting product development

Expedited Scientific Advice – Experience, Pilot Analysis

- Launched March 2023 as 12-month pilot
- Planned analyses: number of requests, scope, questions, outcome (clarification/expedited/standard), product type, committees/WP consulted, expedited procedure duration
- Preliminary experience of 3 expedited requests:

Request	Scope	Question(s)	Expedited criteria met	Outcome	Reason	Conclusion day	Submission to outcome
1	Clinical	Statistical analysis/statistical methods	yes	Expedited SA		day 34	6 weeks
2	Clinical	Statistical analysis/statistical methods	Yes	Expedited SA		day 35	6 weeks
3	Quality/Non-clinical	Comparability programme	Yes	Standard SA	Rapporteur team capacity to initiate review	ongoing	ongoing

- Questionnaire to Rapporteur/SAWP/PRIME product developers at conclusion of pilot:
  - Experience of the procedure, effectiveness, areas for improvement
  - EMA will consult industry on survey content and approach through PRIME contact points

Increasing predictability for regulatory interactions: Regulatory Roadmap and Development tracker

- New basis for tracking and informing EMA/Rapporteur on development status and planned interactions
- Supports kick off meeting, submission readiness meeting
- Provides high-level overview of key development aspects, minimising admin burden
- Aim:
  - Facilitate Rapporteur involvement through predictable regulatory interactions
  - Effective tracking and oversight of ongoing and emerging development issues

New in this update:	**Area**	**Summary of the topic** (brief description)	**Milestones**	**Impact on evidence generation** Low Med High	**Company observations**	**SA planned/advised** (target date if known)	IRIS case number of previous **SA/PIP/OD/ ITF** on the topic
	II. NON-CLINICAL						
Impact lowered	Carcinogenicity	Requirement to perform rodent carcinogenicity study	Weight of evidence assessment following completion of 6 month repeat dose study	**LOW**	Findings from 6 month study consistent with 13 weeks study	No	EMA/SA/0000 123456

Development tracker – Experience, Pilot Analysis

- Launched March 2023 as 12-month pilot (duration dependent on gathered experience)
- Planned analyses: number of trackers submitted, number of updates submitted, metrics compared to previous annual update.
- Preliminary EMA observations:
    - High level of quality, detail, comprehensiveness
    - Companies sought PRIME team support on tracker, incorporated changes
    - Edits on structure recommended prior to circulation to Rapporteurs
- Questionnaire to PRIME product developers/Rapporteurs/regulators at conclusion of pilot:
    - Company experience populating/maintaining the tracker, user-friendliness, effectiveness to support internal processes, effort/administrative burden
    - Utility of the tracker: supporting continuity through kick-off meeting, development milestones, submission readiness meeting
    - Suggestions for improvement
    - EMA will consult industry on survey content and approach through PRIME contact points

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Strengthening engagement: Submission Readiness Meeting

Recognition that >50% PRIME MAAs start as AA but revert to standard TT

Industry and regulator surveys: strengthen engagement in the period between Kick-Off meeting and MAA

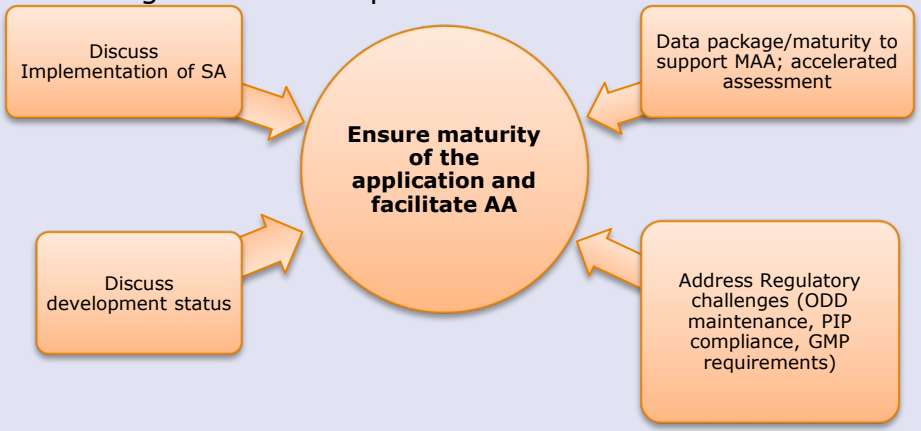
Mirrors opening kick-off meeting format and participants

Supportive documentation – briefing book, draft RMP if available, draft AA request if data available, other documentation (e.g. IMPD) if/as needed

Applicant contacts PRIME team 15 month prior to MAA for meeting 9-12 months prior

MAA pre-submission meeting may still be organised

Applicants are encouraged to make use of the pre-submission interactions with the Agency



Submission readiness meeting – Experience, Pilot Analysis

- Launched March 2023 as 18-month pilot (duration dependent on gathered experience)
- First submission readiness meetings planned September 2023
- Planned analyses: number of meeting held, number of subsequent pre-sub meetings held, analysis of AA outcome and maintenance, MAA duration and outcome.
- Questionnaire to each PRIME product developers/Rapporteurs/EMA at conclusion of pilot:
    - effectiveness (strengthened engagement, identification of outstanding issues, AA/MAA preparedness)
    - Utility of the meeting versus pre-submission activities
    - Suggestions for improvement
- EMA will consult industry on survey content and approach through PRIME contact points

PRIME onboarding to IRIS

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- 3 processes onboarded to IRIS on the 10th of July:
  - Application for PRIME eligibility,
  - Transfer PRIME regulatory entitlement
  - Withdrawal of PRIME regulatory entitlement (RE)
- In September, 2 more processes to be onboarded:
  - PRIME meeting request
  - PRIME Periodic update submission

IRIS PORTAL LOG IN - Home · IRIS (europa.eu)

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Quick interactive guide to IRIS registration process (europa.eu)

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IRIS

Home | Forums | Reg. Entitl. | Products | Cases | Committee Meeting cases | Documents | Network Subm. | Anna Gross

Please note that the Forums are temporarily unavailable. Please submit support requests via the EMA Service Desk.

Access & submission

To use IRIS as a logged-in user to submit your application, you need to complete a few registration steps. A quick interactive guide to the IRIS registration process provides you with a summary of actions to ensure that:

✓ You have an **active EMA account**

✓ Your **organisation is registered** in EMA's Organization Management Service (OMS)

✓ You have the **appropriate user access role and affiliation** to an organization

✓ You have a valid **Research Product Identifier** (RPI) for scientific applications such as orphan designation, scientific advice or ITF

✓ You have a **customer account number** if your application requires a fee.

For more detailed information describing each of the registration steps including the log-in refer to the IRIS guide to registration. To send your submission, follow the instructions contained in the IRIS guide for applicants (scientific applications for industry and individual applicants) and IRIS guide for parallel distribution applicants.

If you wish to discuss anything other than a new medicinal product with the ITF (e.g. a new technology, a group of products or other subject) you should contact itfsecretariat@ema.europa.eu for assistance in obtaining an RPI.

PRIME onboarding to IRIS – Choose Submission type

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New Draft Submission

1 Choose Applicant Type ✔ | 2 Choose Submission Type | 3 Add Managers & Contributors

Select the organisation on behalf of which you are applying *

European Medicines Agency

The choice field above allows you to choose one of the organisations recorded in SPOR-OMS to which you are affiliated. You can request affiliation to an organisation via the EMA Account Management System. Registration of new organisations in SPOR-OMS is done via EMA Servicedesk.

Location *

European Medicines Agency

Submission Type *

Application for PRIME Eligibility

Previous | Create and Next

Lookup records

prime

Application for PRIME Eligibility	To apply for PRIME designation	PRIME
PRIME Meeting Request	To request a meeting following the granting of a PRIME regulatory entitlement (full or early entry)	PRIME
PRIME Periodic Update Submission	To report on changes critical to product development or evidence generation challenges following the granting of full PRIME status.	PRIME
Transfer of PRIME Regulatory Entitlement	To transfer a PRIME regulatory entitlement to a different company and allow them to submit a PRIME meeting request/Withdrawal/ Periodic update for that product.	PRIME
Withdrawal of PRIME Regulatory Entitlement	To request a withdrawal for the PRIME regulatory entitlement	PRIME

Select | Cancel | Remove value

PRIME onboarding to IRIS – Administrative Information

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Submission Form

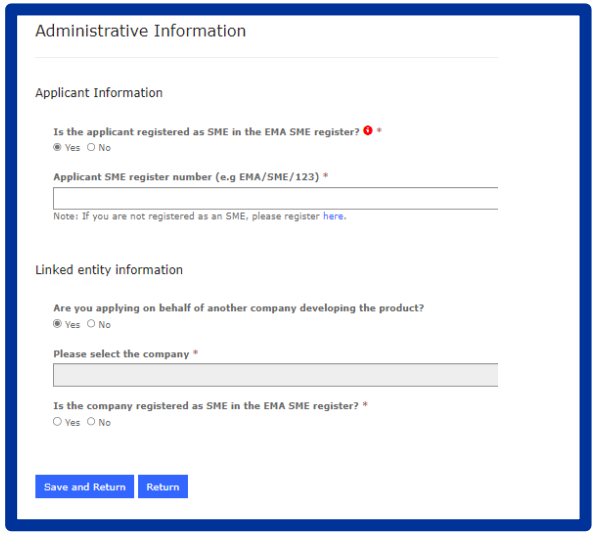
Application for PRIME Eligibility
Reference: EMA/PR/0000073554

Please make sure that the required sections have a green tick to the right (except "Documents from EMA") before submitting the application.
Customer Name : European Medicines Agency
Address : Domenico Scarlattilaan 6 1083 HS Amsterdam Netherlands

- Administrative Information
- Select RPI
- Product Information
- Procedural Information
- Scientific Information
- Submission Notes
- Documents from Applicant
- Documents from EMA
- Submit Application

Return

Generate Application Form



PRIME onboarding to IRIS – Product Information

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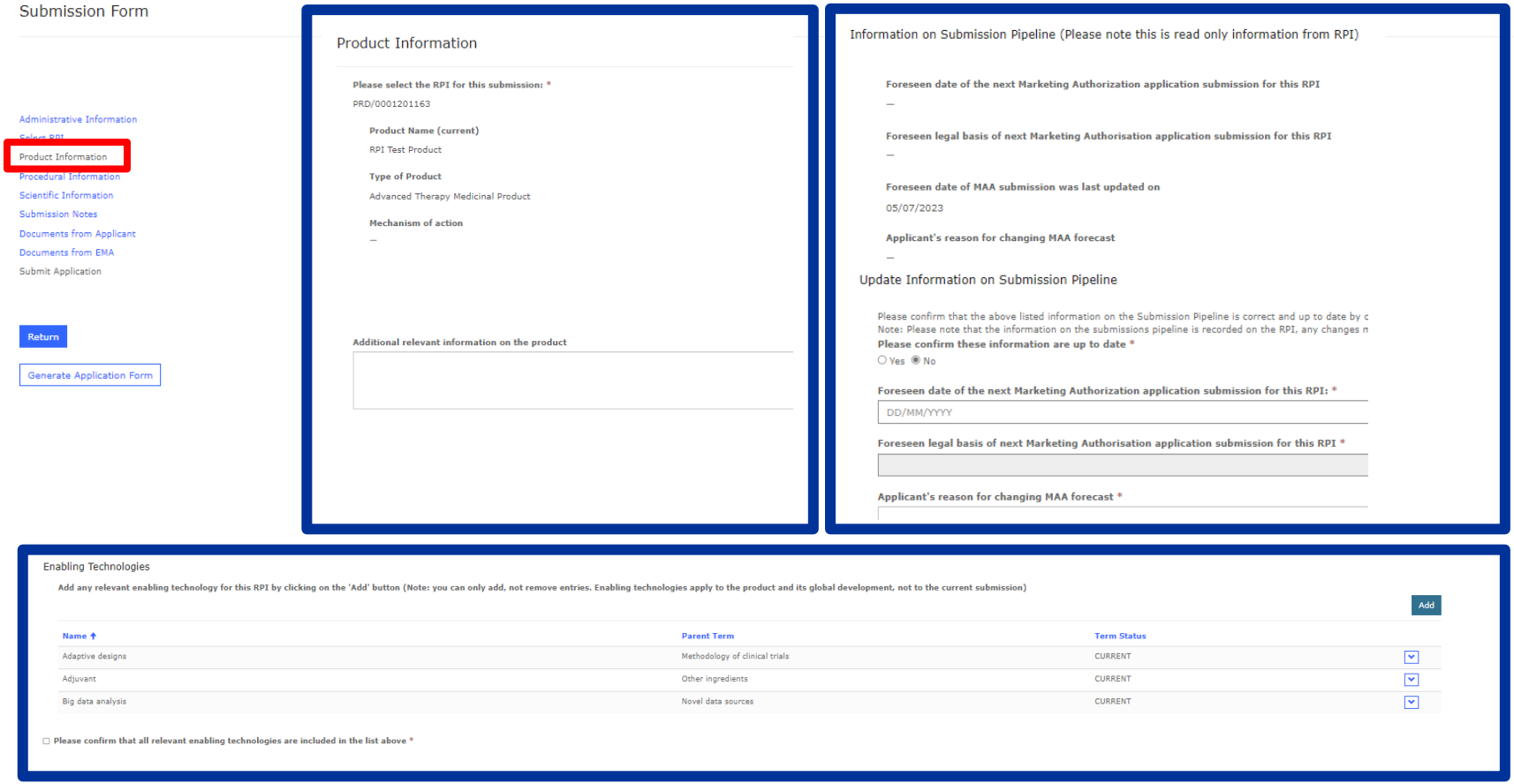

PRIME onboarding to IRIS – Procedural Information

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Submission Form

Administrative Information
Select RPI
Product Information
Procedural Information
Scientific Information
Submission Notes
Documents from Applicant
Documents from EMA
Submit Application

Return

Generate Application Form

Procedural Information

PRIME Submission

Does this product currently hold Early Entry PRIME designation? *
Yes No

Is this a resubmission of a previously denied/withdrawn PRIME eligibility request? *
Yes No

Was a PRIME eligibility pre-submission meeting held prior to the current submission? *
Yes No

Has National Scientific Advice been provided? *
Yes No

Reference Number	Country Advice Received
There are no records to display.	

Has Breakthrough Designation (FDA) been granted? *
Yes No

Is this product included in other international expedited development pathways? (eg. Sakigake, ILAP)
Yes No

Information on Orphan Desgination

Does this product currently have an orphan designation in the condition relevant to this submission? *
Yes No

Information on Paediatric Investigation Plan

Has a PIP or Waiver ever been submitted for this product? *
Yes No

Information on eligibility for the centralised procedure

Has eligibility to the centralised procedure been confirmed? *
Yes No

Save and Return | Return

PRIME onboarding to IRIS – Scientific Information

EUROPEAN MEDICINES AGENCY

Submission Form

Application for PRIME Eligibility
Reference: EMA/PR/0000073554

Please make sure that the required sections have a green tick to the right (except "Documents from EMA") before submitting the application.
Customer Name : European Medicines Agency
Address : Domenico Scarlattilaan 6 1083 HS Amsterdam Netherlands

Administrative Information
Select RPI
Product Information
Procedural Information
Scientific Information
Submission Notes
Documents from Applicant
Documents from EMA
Submit Application

Return

Generate Application Form

Scientific information

Information on the condition to be treated

Proposed scope *

Proposed Condition/Indication

Proposed Condition/Indication (MedDRA) *

Please select the type of data supporting the PRIME application (select all the apply) *

Select or search options

Medical Device

Is a medical device incorporated, as an integral part? *

Yes No

Companion diagnostic

Is the medicinal product to be used with a companion diagnostic within the meaning of Article 2(7) of Regulation *

Yes No

PRIME onboarding to IRIS – Network Portal view

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This view contains all cases associated to at least one Meeting of the SAWP-H. You can filter the data by meeting and other criteria. In text filters, use the asterisk (*) before the search string to increase sensitivity.
Click "Apply" to apply all filters. Click "Export" to download the list as an Excel file (CSV).

Recent/next meetings | Case number | Subject/Active substance(s) | Rapp/CoRapp | Condition

Case status
- ☐ Active
- ☐ Resolved
- ☐ Canceled

Case sub-status
- ☐ Submitted
- ☐ In Progress
- ☐ Submission documents final
- ☐ Start of procedure
- ☐ Under Evaluation by EMA
- ☐ For List of Questions/Opinion

More

Case type
- ☑ Application for PRIME Eligibility
- ☐ Initial Scientific Advice - Human
- ☐ Initial Protocol Assistance
- ☐ Follow up Scientific Advice - Human
- ☐ Follow up Protocol Assistance
- ☐ Initial Qualification Procedure

More

Apply

Search | Export

Case number	Case Type	Sub-status	Subject/Active substance(s)	Submission Folder	Case Folder	Condition	Rapporteur	Co-Rapporteur	Scientific Officer	Applicant	Start Date	Therapeutic area (Scientific Content)	Modified On
EMA/PR/0000071955	Application for PRIME Eligibility	Under Evaluation by EMA		link	link	danon disease	André Elferink		Vanessa Seguin	European Medicines Agency	06/02/2023	Congenital, familial and genetic disorders	01/06/2023 5:04 PM
EMA/PR/0000071218	Application for PRIME Eligibility	Positive		link	link	Hormone Analysis	André Elferink		Lorenzo Guizzaro		17/04/2023	Congenital, familial and genetic disorders	05/07/2023 8:42 PM

PRIME onboarding to IRIS – useful links and next steps

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Supporting material:

1, Industry public DEMO is available on EMA website from the 22nd of June (PRIME eligibility, withdrawal and transfer of RE)

2, Network user guidance folder in Committee Library (Sharepoint)

3, Update of PRIME landing page on EMA website on how to apply via IRIS

4, Update of PRIME Guidance to applicants

Next steps:

1, System DEMO on next processes in September

2, Further update of Guidance documents

Any questions?

Further information

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Send us a question Go to www.ema.europa.eu/contact

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