EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Electronic product information (ePI) in centralised procedures

Guide for applicants in the ePI pilot

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Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
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1. Purpose and context

1.1. Purpose of this guide

This guide is for applicants participating in the ePI pilot. It presents the electronic product information (ePI) process that will be used during the pilot within centralised procedure timeframes and provides details on its practical implementation. **The guide relates only to ePI and does not replace current regulatory guidelines.**

1.2. Preliminary requirements

For ePI creation in the Product Lifecycle Management (PLM) Portal, you will need an active EMA account, ePI user access role(s) and the organisation you are working for listed in OMS and assigned to that account.

Important note: ePI roles are currently only available to participants in the ePI pilot.

- EMA Account Management is the online platform to request and manage your EMA account
- The ePI registration guide describes the steps to request ePI roles in the PLM portal
- The ePI user guide for applicants shows users how to create and manage ePI in the PLM portal

2. Type IA and Type IB variations

2.1. ePI creation prior to submitting application

In case the type IA/type IAIN/type IB variation affects any of the product information annexes, i.e. summary of product characteristics (SmPC), annex II, labelling and/or package leaflet:

- **If no ePI exists for the medicine**:
  prior to submitting the application, the applicant should create an ePI (including SmPC, annex II, labelling and package leaflet) in the PLM Portal by:
  - On the PLM homepage, selecting '*New ePI*' and
  - On the '*Select ePI details*' page, for '*ePI type*' *selecting* '*New ePI*'.

  At the time of submission, the content of the ePI should be identical to the content of the PI in PDF (clean) format included in the eCTD.
- **If an ePI already exists for the medicine**:
  prior to submitting the application, the applicant should create an ePI in the PLM Portal by:
  - On the PLM homepage, selecting '*New ePI*' and
  - On the '*Select ePI details*' page, for '*ePI type*' *selecting* ' *Existing ePI'*, and then selecting the existing ePI (the most recent ePI for the product) to update.

  At the time of submission, the content of the ePI should be identical to the content of the PI in PDF (clean) format included in the eCTD.

Only the English-language version of the ePI is required.

While the ePI is being created, the ePI has the status '*Draft*'. Before the application is submitted, the applicant must change the ePI status to '*Submission*'.

Changing the ePI status from '*Draft*' to '*Submission*' requires that a declaration is completed and signed by a Signatory who is an authorised contact for the product or an alternative company representative.

Since the procedure number will only be assigned by EMA upon receipt of the eCTD application, the procedure number field of the ePI should be completed or edited by the applicant when the number is available.

The applicant must add the procedure number to the ePI before the end of procedure.

2.2. ePI submission and validation

In the cover letter accompanying the type IA/type IB variation notification, the applicant should provide the related ePI ID obtained from the PLM portal by including the following sentences:

> An electronic version of the product information (ePI) in EN has been created to accompany this submission with the ePI ID: {EPI ID in format EPI/YY/XXX copied from PLM portal}
>
> [In case the ePI is an update of an existing ePI, include the sentence:] {On publication, this ePI should replace the existing ePI with the ePI ID: {EPI ID of existing ePI in format EPI/YY/XXX ID copied from PLM portal}.}

During validation before the start of the procedure, the Agency will check that the ePI with the ePI ID provided in the cover letter is present in the PLM portal with the status '*Submission*'. Issues identified with ePI during validation will be notified to the applicant via e-mail. The applicant will be requested to provide responses to the issues raised within 4 working days (Type IA) or 5 working days (Type IB). Delayed or insufficient responses may lead to the application proceeding without inclusion of ePI.

Provision of ePI does not negate the requirement to submit product information annexes in eCTD. The relevant complete set of product information annexes must be submitted in Word and PDF formats in the eCTD sequence and working documents folder as described in the post-authorisation guidance.

The ePI format is not assessed and it is the responsibility of the applicant to ensure that, at the end of the procedure, the ePI is identical in content to the final PI in Word and PDF formats.

Please note: The PLM portal includes a functionality to export ePI to Word, which applicants may wish to utilise for generation of Word files for eCTD submission.

Please note: ePI can only be edited in '*Draft*' status. At any time during the procedure, the applicant can change the ePI from '*Submission*' to '*Draft*' status to enable editing.

2.3. ePI update

The Agency will notify the applicant about the outcome of the review. The ePI may need to be amended as follows:

- **Outcome is favourable and no changes are needed to the submitted ePI**:
  ePI remains in '*Submission*' status until publication. No action needed by applicant.
- **Outcome is favourable and changes are needed to the submitted ePI**:
  Changes to the submitted ePI may be needed, either:
  - as an outcome of the review
  - due to a Validation Request for Supplementary Information (VSI)
  - due to a Request for Supplementary Information (RSI) in a type IB procedure

ePI can only be edited in '*Draft*' status. At any time during the procedure, the applicant can change the ePI from '*Submission*' to '*Draft*' status to enable editing.

By the end the procedure, the applicant must make all necessary edits to the ePI, sign and save the final ePI with the '*Update*' status.

- **Final outcome is unfavourable or application is withdrawn**:
  Within a fortnight after withdrawing or being notified of the unfavourable outcome, the applicant must change the status of the ePI for the procedure to '*Deactivated*' in the PLM portal.

Provision of ePI does not negate the requirement to submit product information annexes in eCTD. The relevant complete set of product information annexes must be submitted in Word and PDF formats in the eCTD sequence and working documents folder as described in the post-authorisation guidance.

2.4. ePI publication

In the case of a favourable outcome, the Agency will mark the ePI as approved in the PLM portal. This is not visible to the applicant in the PLM portal.

At the same time as publication of the PI PDF on the EMA website, the Agency will publish the ePI to the ePI repository, from where it will be publicly available via the ePI application programming interface. The status of the ePI in the PLM portal will change to '*Published*'.

3. Type II variations

3.1. ePI creation prior to submitting application

In case the type II variation affects any of the product information annexes, i.e. SmPC, annex II, labelling and/or package leaflet:

- **If no ePI exists for the medicine**:
  prior to submitting the application, the applicant should create an ePI (including SmPC, annex II, labelling and package leaflet) in the PLM Portal by:
  - On the PLM homepage, selecting '*New ePI*' and
  - On the '*Select ePI details*' page, for '*ePI type*' *selecting* '*New ePI*'.

  At the time of submission, the content of the ePI should be identical to the content of the PI in PDF (clean) format included in the eCTD.
- **If an ePI already exists for the medicine**:
  prior to submitting the application, the applicant should create an ePI in the PLM Portal by:
  - On the PLM homepage, selecting '*New ePI*' and
  - On the '*Select ePI details*' page, for '*ePI type*' *selecting* ' *Existing ePI'*, and then selecting the existing ePI (the most recent ePI for the product) to update.

  At the time of submission, it is not necessary for the content of the ePI to be identical to the content of the PI in PDF (clean) format included in the eCTD.

  Important note: For updates of existing ePIs, it is not necessary for the content to be identical to the eCTD submitted PDF. This is to avoid duplication of effort for applicants preparing Word PI with track changes in parallel. Applicants can instead include all changes in the final ePI at the end of the procedure.

Only the English-language version of the ePI is required.

While the ePI is being created, the ePI has the status '*Draft*'. Before the application is submitted, the applicant must change the ePI status to '*Submission*'.

Changing the ePI status from 'Draft' to 'Submission' requires that a declaration is completed and signed by a Signatory who is an authorised contact for the product.

Since the procedure number will only be assigned by EMA upon receipt of the eCTD application, the procedure number field of the ePI should be completed or edited by the applicant when the number is available.

The applicant must add the procedure number to the ePI before the end of procedure.

3.2. ePI submission and validation

In the cover letter accompanying the type II variation notification, the applicant should provide the related ePI ID obtained from the PLM portal by including the following sentence:

> An electronic version of the product information (ePI) in EN has been created to accompany this submission with the ePI ID: {EPI ID in format EPI/YY/XXX copied from PLM portal}
>
> [In case the ePI is an update of an existing ePI, include the sentence:] {On publication, this ePI should replace the existing ePI with the ePI ID: {EPI ID of existing ePI in format EPI/YY/XXX ID copied from PLM portal}.}

During validation (between the submission date and the start date of the procedure), the Agency will check that the ePI with the ePI ID provided in the cover letter is present in the PLM portal with the status '*Submission*'. Issues identified with ePI during validation will be notified to the applicant via e-mail. The applicant will be requested to provide responses to the issues raised within 5 working days. Delayed or insufficient responses may lead to the application proceeding without inclusion of ePI.

Provision of ePI does not negate the requirement to submit product information annexes in eCTD. The relevant complete set of product information annexes must be submitted in Word and PDF formats in the eCTD sequence and working documents folder as described in the post-authorisation guidance.

The ePI format is not assessed and it is the responsibility of the applicant to ensure that, at the end of the procedure, the ePI is identical in content to the final Word and PDF formats.

Please note: The PLM portal includes a functionality to export ePI to Word, which applicants may wish to utilise for generation of Word files for eCTD submission.

Please note: ePI can only be edited in '*Draft*' status. At any time during the procedure, the applicant can change the ePI from '*Submission*' to '*Draft*' status to enable editing.

3.3. ePI update

Following the assessment of the variation and on the day of the CHMP opinion on the variation is adopted, the ePI may need to be amended as follows:

- **Outcome is favourable and no changes are needed to the submitted product information**: ePI remains in '*Submission*' status until publication. No action needed by applicant.
- **Outcome is favourable and changes are needed to the submitted product information**: Changes to the submitted ePI may be needed, either:
  - as an outcome of the review

- because the ePI was created based on an existing ePI and all updates were not already included in the submitted ePI.

ePI can only be edited in '*Draft*' status. At any time during the procedure, the applicant can change the ePI from '*Submission*' to '*Draft*' status to enable editing.
By the end of the linguistic review (I.e. 25 days after the CHMP plenary meeting where the opinion was adopted) the applicant must make all necessary edits to the ePI, sign and save the updated ePI with the '*Update*' status.

- **Outcome is unfavourable and re-examination requested**:
  If the applicant will request a re-examination, the ePI can be in any status pending the final outcome of the procedure. If the outcome of the re-examination is favourable, see points above. If the outcome is unfavourable, see below.
- **Final outcome is unfavourable**:
  Within 5 days after the unfavourable opinion, the applicant must change the status of the ePI for the procedure to '*Deactivated*' in the PLM portal.
- **Application is withdrawn:**
  If the applicant decides to withdraw, within 5 days after notifying the Agency of the withdrawal, the applicant must change the status of the ePI for the procedure to '*Deactivated*' in the PLM portal.

Provision of ePI does not negate the requirement to submit product information annexes in eCTD. The relevant complete set of product information annexes must be submitted in Word and PDF formats in the eCTD sequence and working documents folder as described in the post-authorisation guidance.

3.4. ePI publication

In the case of a favourable opinion, after day +25 (for variations not requiring amendment to the Commission Decision) or at the time of the Commission Decision, the Agency will mark the ePI as approved in the PLM portal. This is not visible to the applicant in the PLM portal.

At the same time as publication of the PI PDF on the EMA website, the Agency will publish the ePI to the ePI repository, from where it will be publicly available via the ePI application programming interface. The status of the ePI in the PLM portal will change to '*Published*'.

4. Renewal (5 year)

4.1. ePI creation prior to submitting application

ePI must be created for 5-year renewal applications, even when no changes are proposed to PI, as follows:

- **If no ePI exists for the medicine**:
  prior to submitting the application, the applicant should create an ePI (including SmPC, annex II, labelling and package leaflet) in the PLM Portal by:
  - On the PLM homepage, selecting '*New ePI*' and
  - On the '*Select ePI details*' page, for '*ePI type*' *selecting* '*New ePI*'.

  At the time of submission, the content of the ePI should be identical to the content of the PI in PDF (clean) format included in the eCTD.

- **If an ePI already exists for the medicine**:
  prior to submitting the application, the applicant should create an ePI in the PLM Portal by:
  - On the PLM homepage, selecting '*New ePI*' and
  - On the '*Select ePI details*' page, for '*ePI type*' *selecting* ' *Existing ePI'*, and then selecting the existing ePI (the most recent ePI for the product) to update.

  At the time of submission, it is not necessary for the content of the ePI to be identical to the content of the PI in PDF (clean) format included in the eCTD.

  Important note: For updates of existing ePIs, it is not necessary for the content to be identical to the eCTD submitted PDF: this is to avoid duplication of effort for applicants preparing Word PI with track changes in parallel. Applicants can instead include all changes in the final ePI at the end of the procedure.

Only the English-language version of the ePI is required.

While the ePI is being created, the ePI has the status '*Draft*'. Before the application is submitted, the applicant must change the ePI status to '*Submission*'.

Changing the ePI status from '*Draft*' to '*Submission*' requires that a declaration is completed and signed by a Signatory who is an authorised contact for the product.

Since the procedure number will only be assigned by EMA upon receipt of the eCTD application, the procedure number field of the ePI should be completed or edited by the applicant when the number is available.

4.2. ePI submission and validation

In the cover letter accompanying the renewal application, the applicant should provide the related ePI ID obtained from the PLM portal by including the following sentence:

> An electronic version of the product information (ePI) in EN has been created to accompany this submission with the ePI ID: {EPI ID in format EPI/YY/XXX copied from PLM portal}
>
> [In case the ePI is an update of an existing ePI, even when no changes to the PI are proposed, include the sentence:] {On publication, this ePI should replace the existing ePI with the ePI ID: {EPI ID of existing ePI in format EPI/YY/XXX ID copied from PLM portal}.}

During validation (between the submission date and the start date of the procedure), the Agency will check that the ePI with the ePI ID provided in the cover letter is present in the PLM portal with the status '*Submission*'. Issues identified with ePI during validation will be notified to the applicant via e-mail. The applicant will be requested to provide responses to the issues raised within 5 working days. Delayed or insufficient responses may affect the timely start of the procedure.

Provision of ePI does not negate the requirement to submit product information annexes in eCTD. The relevant complete set of product information annexes must be submitted in Word and PDF formats in the eCTD sequence and working documents folder as described in the post-authorisation guidance. The ePI format is not assessed and it is the responsibility of the applicant to ensure that, at the end of the procedure, the ePI is identical in content to the final Word and PDF formats.

Please note: The PLM portal includes a functionality to export ePI to Word, which applicants may wish to utilise for generation of Word files for eCTD submission.

Please note: ePI can only be edited in '*Draft*' status. At any time during the procedure, the applicant can change the ePI from '*Submission*' to '*Draft*' status to enable editing.

4.3. ePI update

By day 90/120, the CHMP opinion on the renewal is adopted. The ePI may need to be amended as follows:

- **Outcome is favourable and no changes are needed to the submitted product information**: ePI remains in '*Submission*' status until publication. No action needed by applicant.
- **Outcome is favourable and changes are needed to the submitted product information**: Changes to the submitted ePI may be needed, either:
  - as an outcome of the review
  - because the ePI was created based on an existing ePI and all updates were not already included in the submitted ePI.

  ePI can only be edited in '*Draft*' status. At any time during the procedure, the applicant can change the ePI from '*Submission*' to '*Draft*' status to enable editing.
  By day +25 (that is 25 days after the CHMP plenary meeting where the opinion was adopted) the applicant must make all necessary edits to the ePI, sign and save the updated ePI with the '*Update*' status.
- **Outcome is unfavourable**:
  If the applicant will request a re-examination, the ePI can be in any status pending the final outcome of the procedure.
- **Final outcome is unfavourable**:
  Within 5 days after the unfavourable opinion, the applicant must change the status of the ePI for the procedure to '*Deactivated*' in the PLM portal.
- **Application is withdrawn:**
  If the applicant decides to withdraw, within 5 days after notifying the Agency of the withdrawal, the applicant must change the status of the ePI for the procedure to '*Deactivated*' in the PLM portal.

4.4. ePI publication

In the case of a favourable opinion, at the time of the Commission Decision, the Agency will mark the ePI as approved in the PLM portal. This is not visible to the applicant in the PLM portal.

At the same time as publication of the PI PDF on the EMA website, the Agency will publish the ePI to the ePI repository, from where it will be publicly available via the ePI application programming interface. The status of the ePI in the PLM portal will change to '*Published*'.

5. Article 61(3) notifications

5.1. ePI creation prior to submitting application

Article 61(3) procedures affect labelling and/or package leaflet annexes of the product information. ePI must be created as follows:

- **If no ePI exists for the medicine**:
  prior to submitting the application, the applicant should create an ePI (including SmPC, annex II, labelling and package leaflet) in the PLM Portal by:
  - On the PLM homepage, selecting '*New ePI*' and

- On the '*Select ePI details*' page, for '*ePI type*' *selecting* '*New ePI*'.

  At the time of submission, the content of the ePI should be identical to the content of the PI in PDF (clean) format included in the eCTD.

- **If an ePI already exists for the medicine**:
  prior to submitting the application, the applicant should create an ePI in the PLM Portal by:
  - On the PLM homepage, selecting '*New ePI*' and
  - On the '*Select ePI details*' page, for '*ePI type*' *selecting* ' *Existing ePI'*, and then selecting the existing ePI (the most recent ePI for the product) to update.

    At the time of submission, the content of the ePI should be identical to the content of the PI in PDF (clean) format included in the eCTD.

Only the English-language version of the ePI is required.

While the ePI is being created, the ePI has the status '*Draft*'. Before the application is submitted, the applicant must change the ePI status to '*Submission*'.

Changing the ePI status from 'Draft' to 'Submission' requires that a declaration is completed and signed by a Signatory who is an authorised contact for the product.

Since the procedure number will only be assigned by EMA upon receipt of the eCTD application, the procedure number field of the ePI should be completed or edited by the applicant when the number is available.

The applicant must add the procedure number to the ePI before the end of procedure.

5.2. ePI submission and validation

In the cover letter accompanying the 61(3) notification, the applicant should provide the related ePI ID obtained from the PLM portal by including the following sentences:

> An electronic version of the product information (ePI) in EN has been created to accompany this submission with the ePI ID: {EPI ID in format EPI/YY/XXX copied from PLM portal}
>
> [In case the ePI is an update of an existing ePI, include the sentence:] {On publication, this ePI should replace the existing ePI with the ePI ID: {EPI ID of existing ePI in format EPI/YY/XXX ID copied from PLM portal}.}

During validation before the start of the procedure, the Agency will check that the ePI with the ePI ID provided in the cover letter is present in the PLM portal with the status '*Submission*'. Issues identified with ePI during validation will be notified to the applicant via e-mail. The applicant will be requested to provide responses to the issues raised within 5 working days. Delayed or insufficient responses may affect the timely start of the procedure.

Provision of ePI does not negate the requirement to submit product information annexes in eCTD. The relevant complete set of product information annexes must be submitted in Word and PDF formats in the eCTD sequence and working documents folder as described in the post-authorisation guidance. The ePI format is not assessed and it is the responsibility of the applicant to ensure that, at the end of the procedure, the ePI is identical in content to the final Word and PDF formats.

Please note: The PLM portal includes a functionality to export ePI to Word, which applicants may wish to utilise for generation of Word files for eCTD submission.

Please note: ePI can only be edited in '*Draft*' status. At any time during the procedure, the applicant can change the ePI from '*Submission*' to '*Draft*' status to enable editing.

5.3. ePI update

The Agency will notify the applicant about the outcome. The ePI may need to be amended as follows:

- **Outcome is favourable and no changes are needed to the submitted ePI**:
  ePI remains in '*Submission*' status until publication. No action needed by applicant.
- **Outcome is favourable and changes are needed to the submitted ePI**:
  Changes to the submitted ePI may be needed, either:
  - as an outcome of the review
  - due to a Validation Request for Supplementary Information (VSI)

  ePI can only be edited in '*Draft*' status. At any time during the procedure, the applicant can change the ePI from '*Submission*' to '*Draft*' status to enable editing.

  By the end of the procedure, the applicant must make all necessary edits to the ePI, sign and save the final ePI with the '*Update*' status.
- **Final outcome is unfavourable or application is withdrawn**:
  Within a fortnight after withdrawing or being notified that the changes are not accepted, the applicant must change the status of the ePI for the procedure to '*Deactivated*' in the PLM portal.

5.4. ePI publication

In the case of a favourable outcome, at the end of the procedure, the Agency will mark the ePI as approved in the PLM portal. This is not visible to the applicant in the PLM portal.

At the same time as publication of the PI PDF on the EMA website, the Agency will publish the ePI to the ePI repository, from where it will be publicly available via the ePI application programming interface. The status of the ePI in the PLM portal will change to '*Published*'.

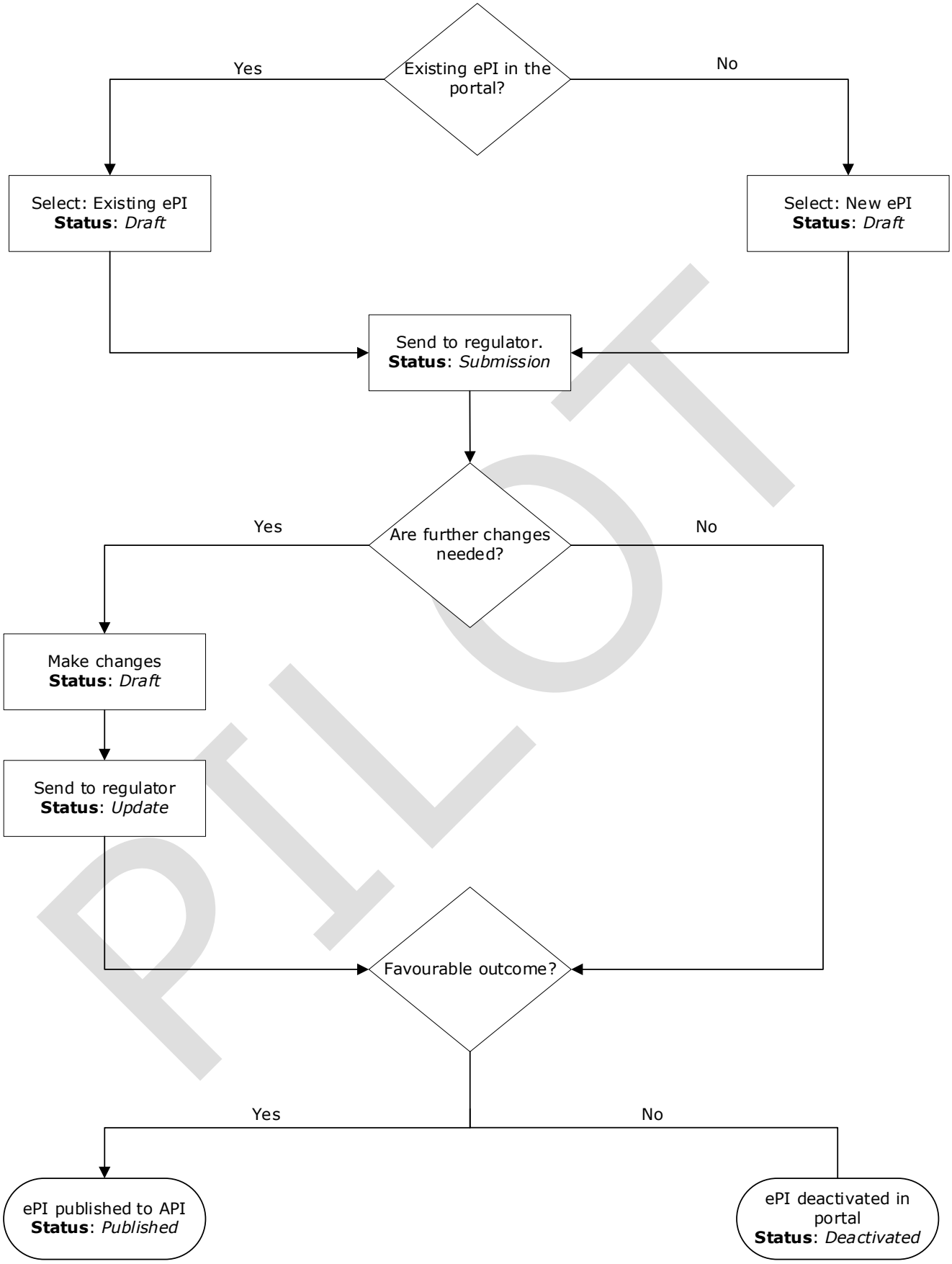

Figure 1. ePI status throughout regulatory procedure.