Health Products and Food Branch

Your Health and Safety - Our Priority

e-Review

Managing Submissions in the eCTD Format: Hybrid Pilot

Sheila Hills / Leane Malone

Therapeutic Products Directorate

February 22, 2006

Health Canada Santé Canada

Canada

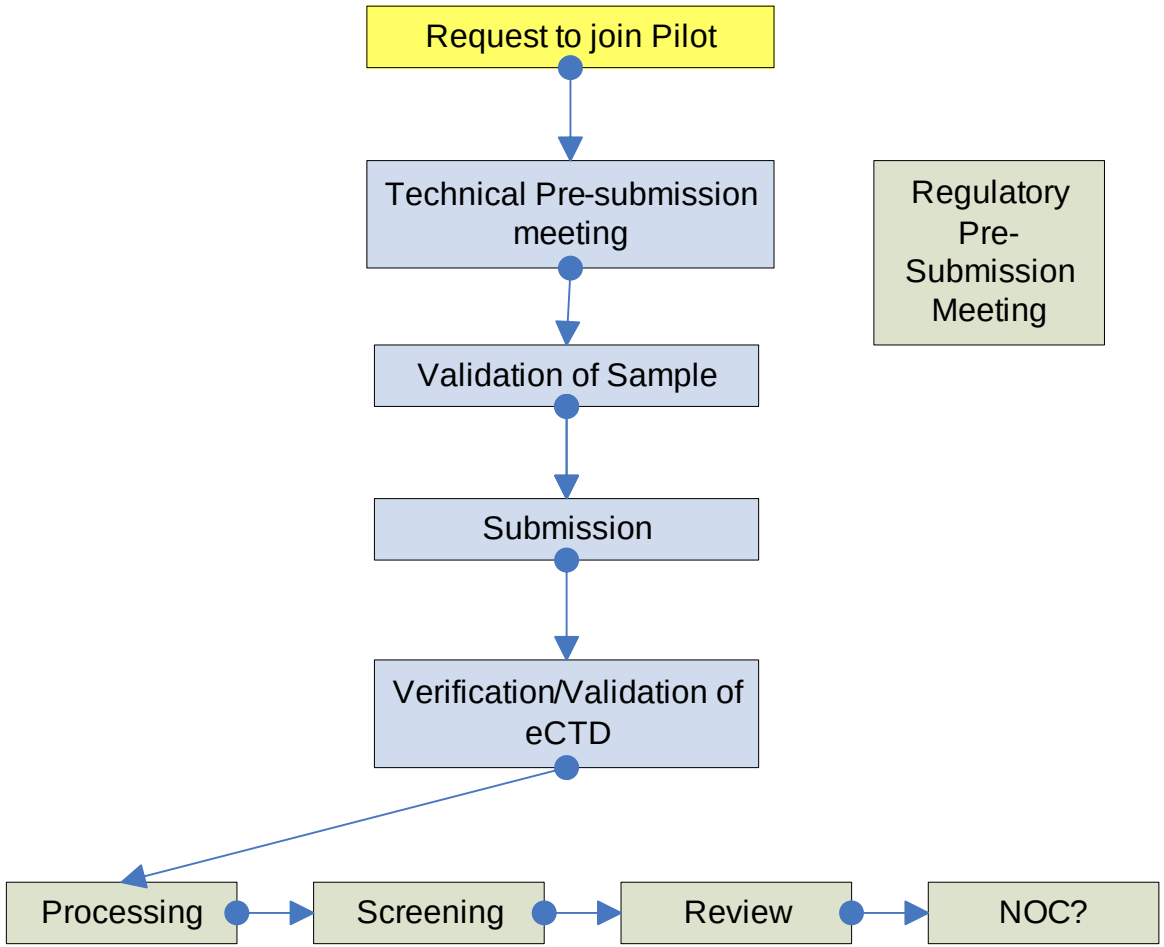
Outline

- Key messages
- Request to participate in the Hybrid Pilot
- Technical meeting requests
- Sample eCTD Validation
- Filing of information and material
- eCTD Validation
- Processing, Screening, Evaluation

Key Messages

- No impact to HC performance targets
- Major change in business
- State of e-readiness varies
- Print-on-demand requests should decrease over time
- Need to work together to resolve validation issues
- Hybrid pilot is an opportunity

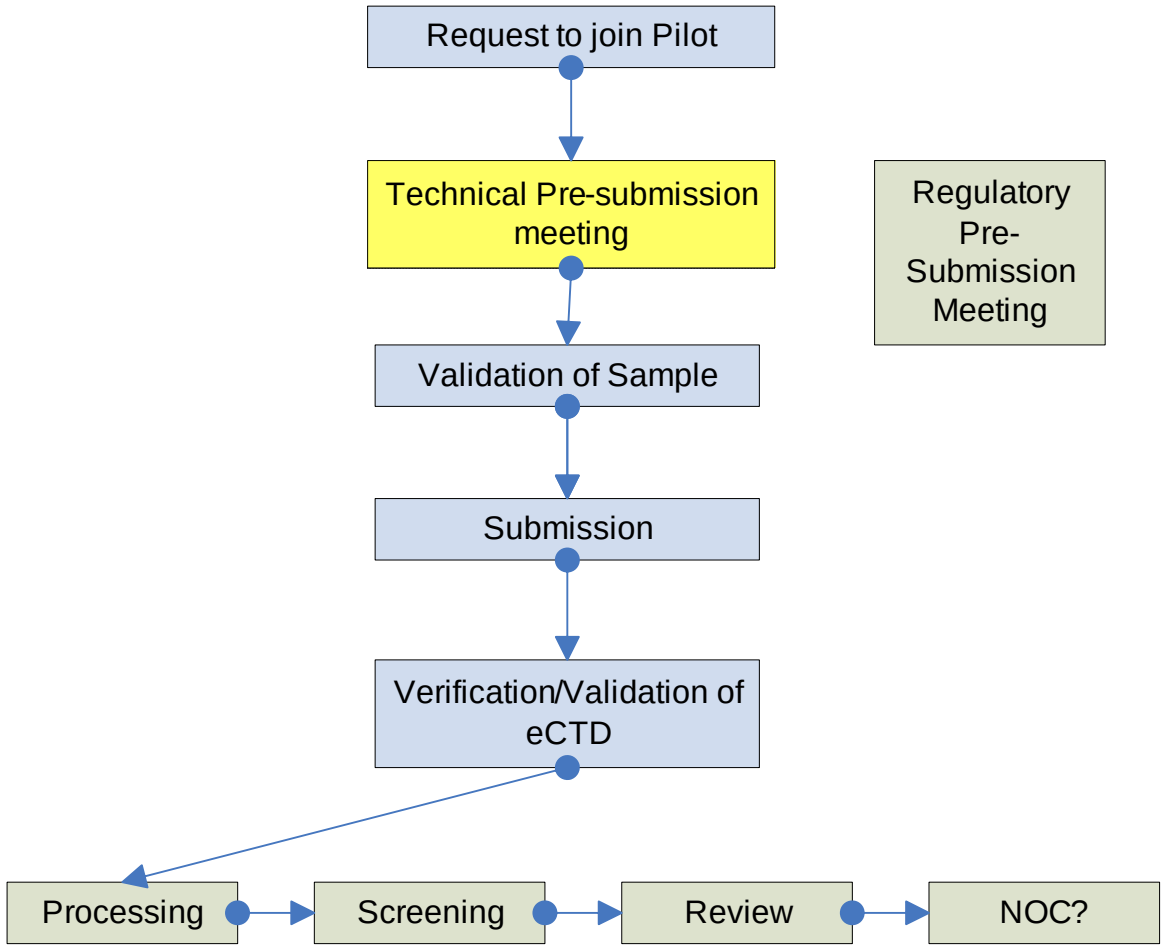
Hybrid Pilot: Overview



Request to Participate

- Refer to Guidance for Industry: Preparation of NDS in eCTD Format (Appendix F)
  - Include the specific information requested
- Request should be sent to SIPD
  - SIPD will review the request to ensure the Appendix F elements have been included
  - SIPD will request any missing information
  - When all the relevant information is received SIPD will officially acknowledge the request
  - Starting June 2006, HC will advise sponsors of their eligibility for the hybrid pilot
    - For requests received before June 1/06 sponsors will be advised of their eligibility before June 15th
    - For requests received on or after June 1/06 sponsors will be advised of their eligibility within 2 weeks of submitting their request
- Decisions regarding participation will not be eligible for reconsideration

Hybrid Pilot: Overview



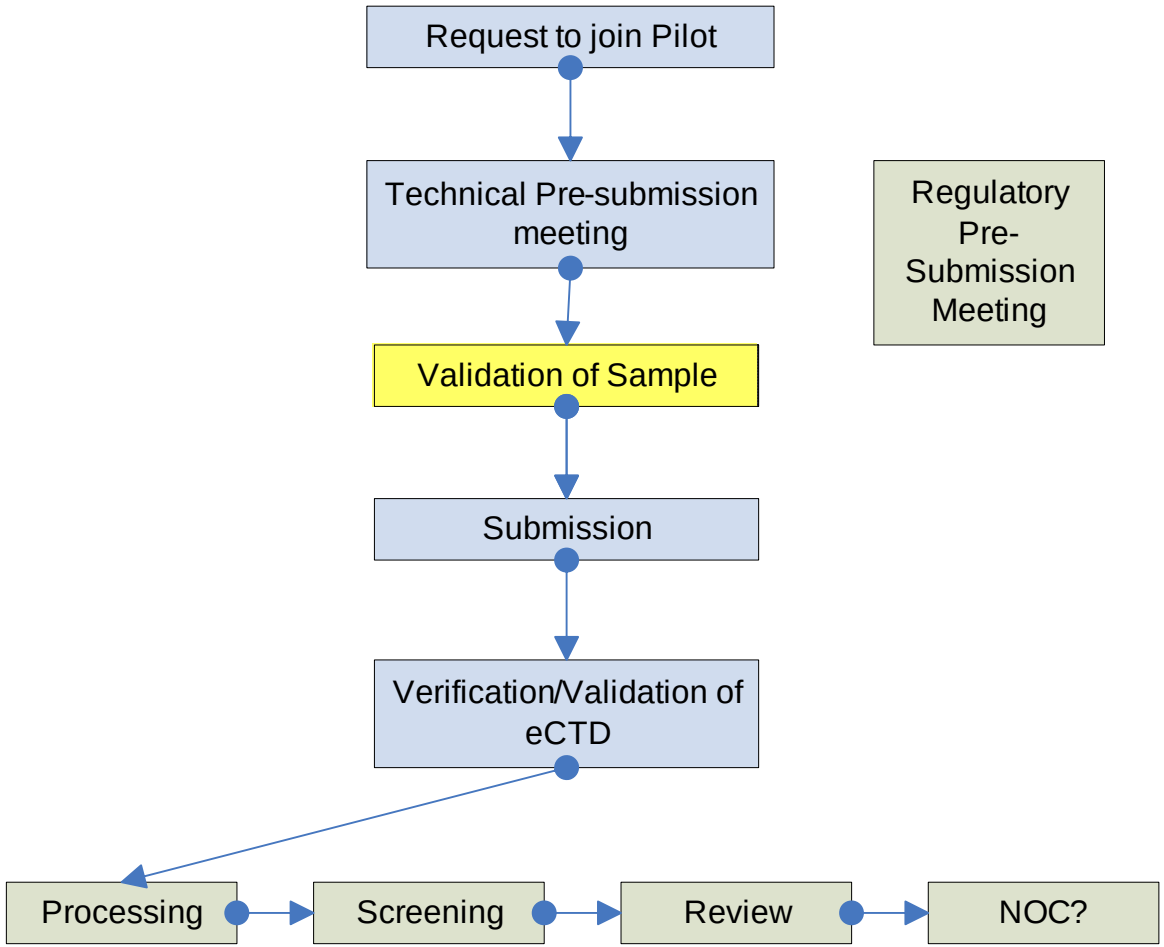
Meeting Requests

- Mandatory technical pre-submission meeting
- To clarify needs, responsibilities, expectations
- Provide assistance and guidance
- May be independent of regulatory pre-submission meeting
  - When requested and where feasible an effort will be made to coordinate the technical and regulatory pre-submission meetings

Technical Meeting Request

- Requests to be submitted to SIPD
- Request in writing, by mail or fax, at least one month prior to the proposed meeting date
- Meeting request should include:
  - Purpose of meeting
  - Proposed agenda
  - Technical questions
  - Proposed meeting dates (option of 3)
- Technical pre-submission meeting package must be submitted at least two weeks prior to the meeting

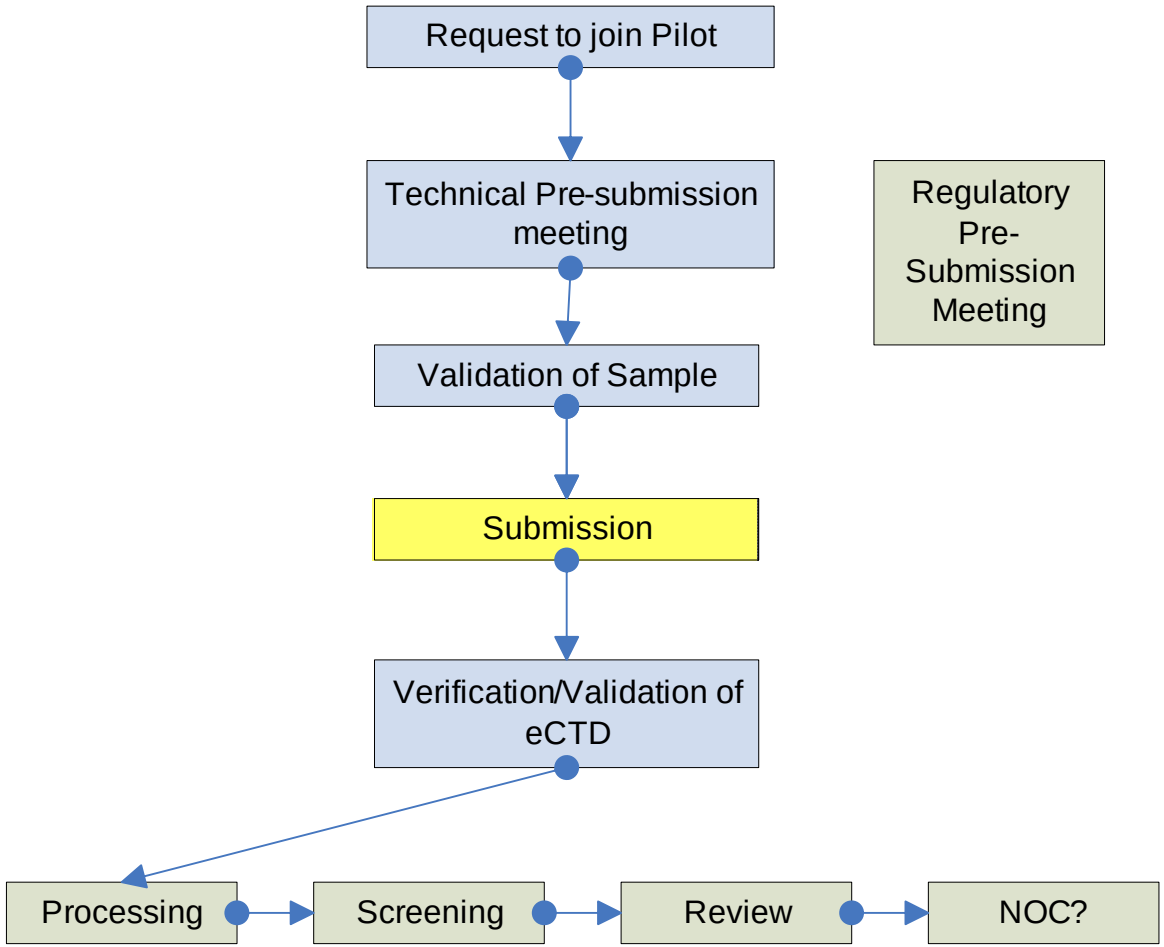
Hybrid Pilot: Overview



Sample eCTD Validation

- Send sample eCTD to SIPD for validation
  - Ensure compatibility between sponsor's software and HC software
- Verification/validation of sample confirmed by HC within 10 days (target 48 hours)

Hybrid Pilot: Overview



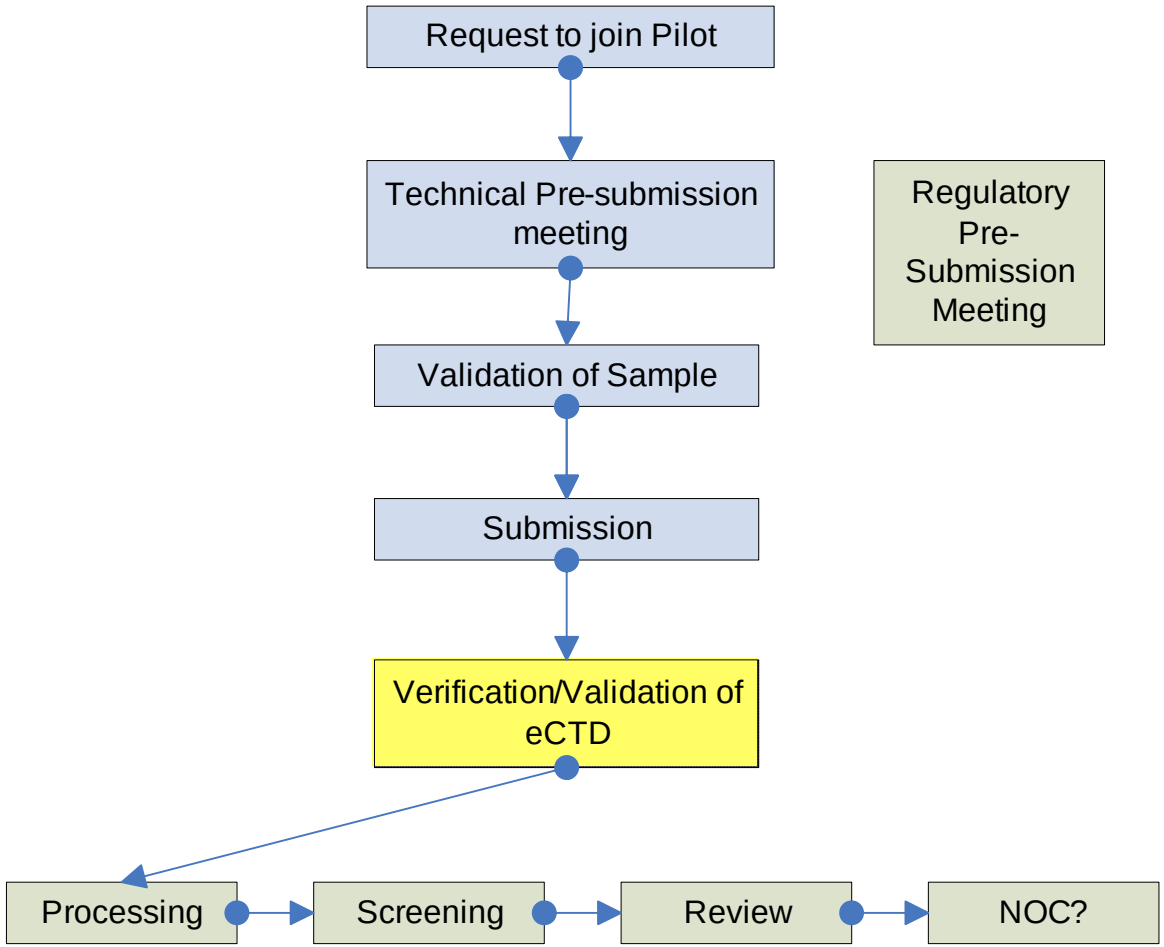
Filing of Information and Material

- Once a submission is filed in eCTD format all additional and subsequent submissions for the same drug product should be filed in eCTD format, including NCs and annual updates
- Sponsors should not revert to the paper-based CTD format as the only filing format
- Subsequent eCTD filing does not apply to CTAs submitted after the NOC is issued
- Hybrid pilot requires the filing of Modules 1,2 in paper CTD format at same time as the complete eCTD is filed

Filing of Information and Material

- eCTD format is encouraged for combination submissions (drug-device) where the primary mechanism of action is drug-related and the device component has been previously approved
- To ensure no loss in review time responses to clarifaxes (screening or review) must be filed in both electronic and paper formats
  - Clarifax response in eCTD format should be filed to SIPD
  - Paper-based clarifax response to be sent to the HC official who requested the information

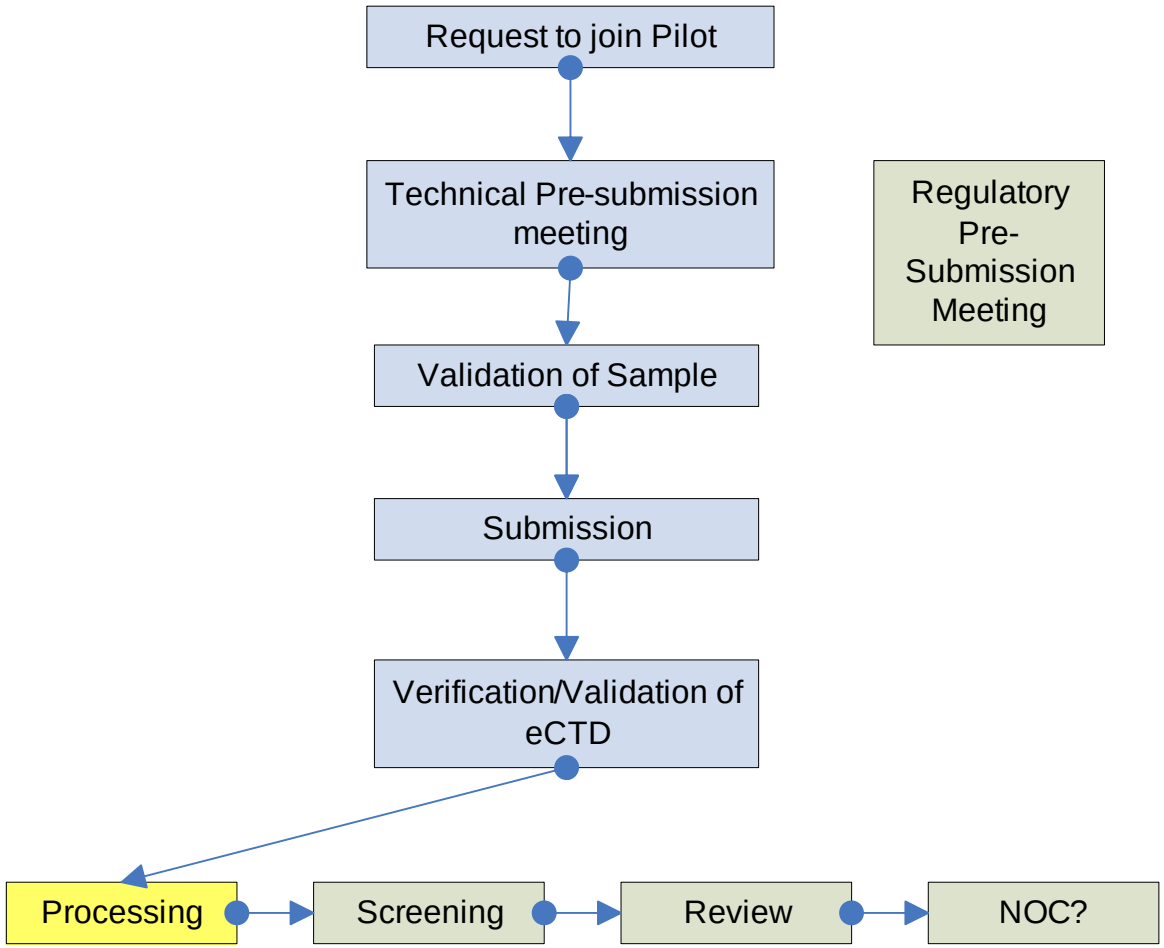
Hybrid Pilot: Overview



eCTD Validation

- eCTD can be filed once sample eCTD has passed validation
- eCTD should be sent to SIPD
- Verification/validation of eCTD confirmed by SIPD within 10 days
  - Process repeats until verification/validation is successful
  - HC assistance and guidance available
- Only when eCTD has passed the verification/ validation process will the submission be acknowledged and **accepted for filing**
- eCTD will be processed by SIPD

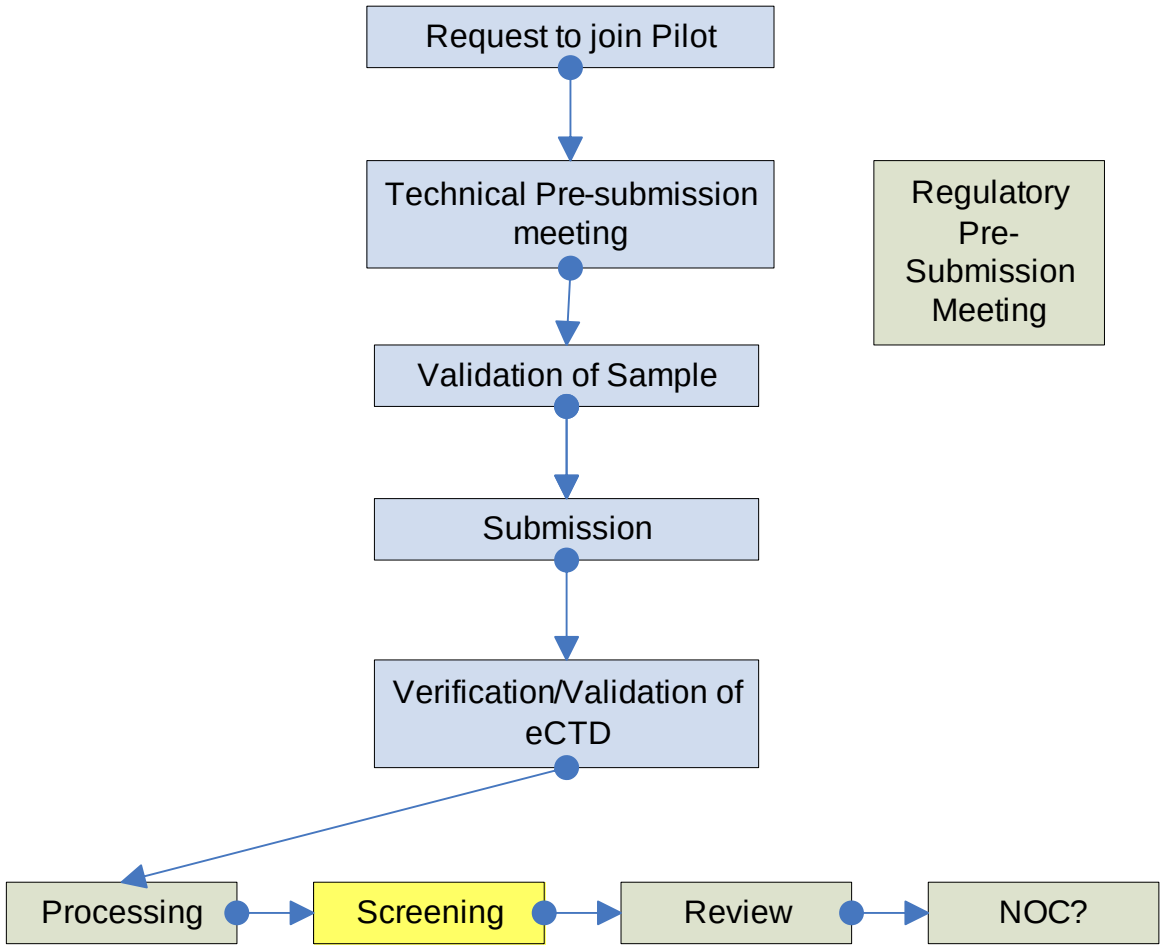
Hybrid Pilot: Overview



Processing of Information and Material

- When the eCTD is acceptable for filing it is then uploaded to the Health Canada secure server
- A central registry (CR) file is opened to hold any paper records, i.e. HC generated paper-based documents, paper-based clarifaxes, etc.
- The file is forwarded to the relevant review Bureau/Center

Hybrid Pilot: Overview



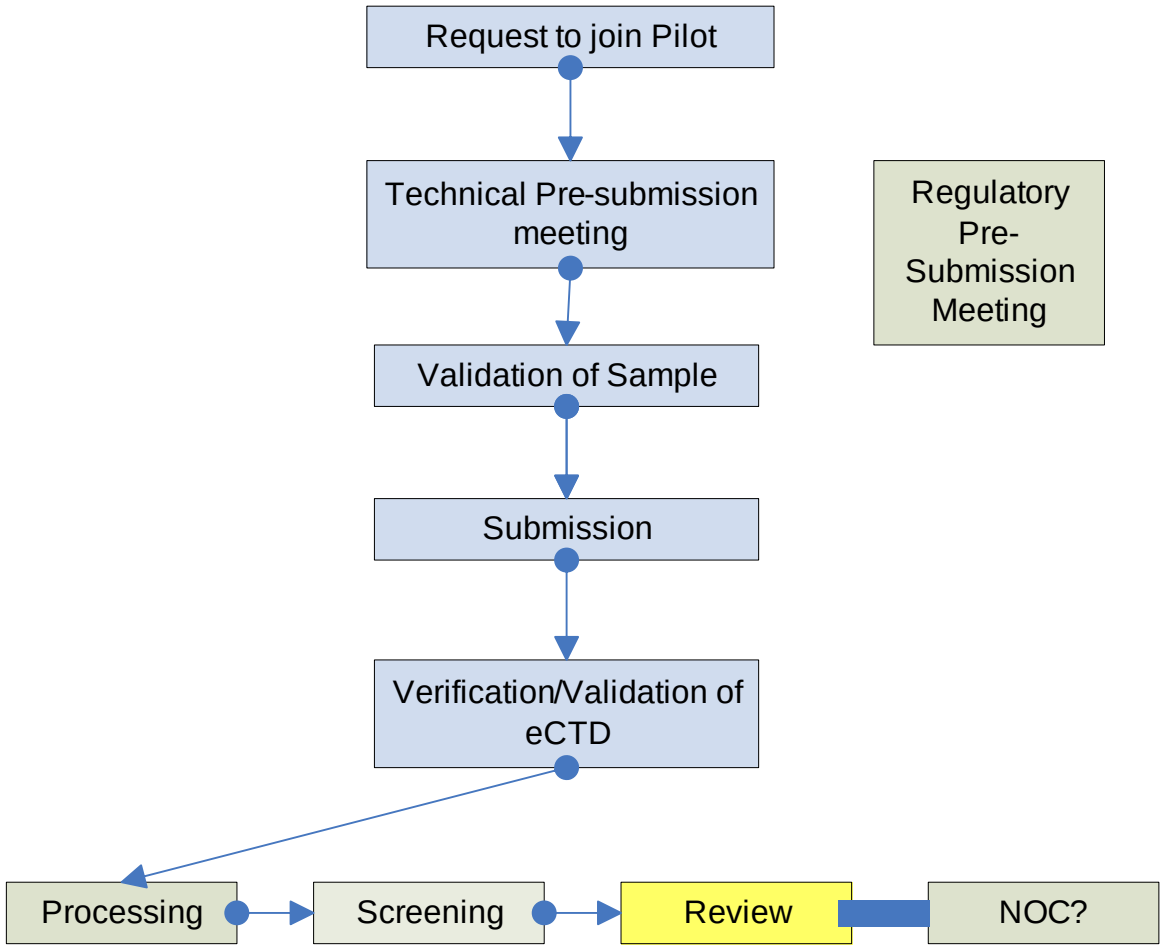
Screening of Information and Material

- Letter of Attestation
  - Confirms content found in eCTD Module 1,2 is identical to the content of Modules 1,2 of the paper-based CTD
  - Include with every sequence where a paper copy is provided
- Original information and material is screened
  - Acceptable
    - Letter of Acceptance issued and the submission proceeds for review
  - Unacceptable
    - Screening clarifax may be issued
      - Response in eCTD format is to be submitted to SIPD
      - Response to clarifax requires an increment to the sequence
      - Response should follow Q and A format
      - Paper-based clarifax response to be sent to the HC official who requested the information

Screening of Information and Material

- Unacceptable (cont'd)
  - Screening Deficiency Notice is issued
    - Clock stops
    - Sponsor has 45 days to respond
    - Response, in eCTD format, should be submitted to SIPD
      - Verification/validation of the response to the SDN confirmed by HC within 10 days (target 48 hours)
      - Process repeats until verification/validation is successful
      - HC assistance and guidance available
    - Only when the response has passed the verification/validation process will the submission be **accepted for processing**

Hybrid Pilot: Overview



Evaluation of Submissions

- Paper-based information and material
  - Instances where urgency requires a paper copy to be filed in addition to the electronic copy,
    - Clarifax responses
      - e.g. Review clarifax, product monograph negotiation
    - Immediate safety concerns
- Letter of Attestation
  - Include with every sequence where a paper copy is provided
- Clarification Requests issued during review
  - Response to be submitted electronically to SIPD
  - Response to clarifax requires an increment to the sequence
  - Response should follow Q and A format
  - Paper response should be submitted directly to HC official who requested the information

Evaluation of Submission

- Notice of Deficiency / Notice of Non-Compliance
  - Clock stops
  - Sponsor has 90 days to respond
  - Response, in eCTD format, should be submitted to SIPD
    - Verification/validation of the response to the SDN confirmed by HC within 10 days (target 48 hours)
    - Process repeats until verification/validation is successful
    - HC assistance and guidance available
  - Only when the response has passed the verification/validation process will the response to the NOD/NON be **accepted for processing**

Print on Demand (POD)

- Sponsors should be prepared to handle large print on demand requests within short time frames
- Sponsors will be contacted by RPMD/RAD prior to the issuance of a formal print on demand request
  - RPMD/RAD will advise the sponsor of who is requesting the POD, the reason for the POD, the specific material to be printed and the expected time line for a response
    - For example, the POD is being requested by Dr. B due to ergonomic reasons; studies X, Y and Z are required and should be submitted within 2 business days
  - The sponsor should advise RPMD/RAD of any difficulty with the request
    - For example, the material requested was previously submitted to HC in a paper-based format
    - Note: availability of resources to print and organize the documents in CTD format will not be accepted as a reason to extend the expected time line
  - RPMD/RAD will issue a formal print on demand request following discussion with the sponsor outlining the necessary logistics

Print on Demand

- POD response should include a copy of the formal POD request and should be sent directly to SIPD
- SIPD will acknowledge receipt of the response and forward to the reviewer identified in the POD request
- Reviewer should ensure the response is complete and advise RPMD/RAD
- If the response is incomplete RPMD/RAD will contact the sponsor for follow-up action
- Statistics will be maintained regarding print on demand requests

Thank you