Health Canada Santé Canada

Guidance on submitting pediatric development plans and pediatric studies

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Canada

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Contents

OVERVIEW **5**

Purpose 5

Background 5

Scope and application 5

Policy objectives 6

Note about guidance documents in general 6

Transparency 7

WHEN TO SUBMIT PLANS AND STUDIES **7**

FOREIGN-APPROVED PLANS **10**

Format and content 10

Canadian addendum *11*

Situations where the foreign decision may not apply 11

EMA class waiver *11*

US FDA orphan drug exemption *12*

Verifying a foreign-approved PDP 12

Amending a foreign-approved PDP 13

CANADIAN PLANS **14**

Format and content 14

Title page *15*

Overview of the disease or condition in the pediatric population *15*

Proposed pediatric development plan *15*

Overview of planned extrapolation to specific pediatric populations *16*

Rationale for not conducting studies *17*

Rationale for not conducting studies based on an adult-related condition that rarely or never occurs in children or is on the EMA class waiver *18*

Adult cancer drugs determined to be substantially relevant to the growth or progression of a pediatric cancer *18*

Tabular summary of planned nonclinical and clinical development *19*

Development of age-appropriate formulation *22*

Nonclinical studies *22*

Clinical data to support design and/or initiation of studies in pediatric patients *23*

Ongoing and planned pediatric studies *23*

Agreements for pediatric studies with other regulatory authorities *24*

Reviewing a Canadian PDP 25
Amending an agreed-to Canadian PDP 26
Canadian PDP template 27
ANNUAL REPORTING 27
Filing annual reports 27
Annual reporting for foreign and Canadian PDPs 28
PLANS WITH SUBSEQUENT SNDSS 30
STUDY REPORTS 31
CONTACT US 31

Overview

Purpose

This guidance outlines the policy on submitting a pediatric study. It's intended to help sponsors align their submissions with the policy. The pediatric study submission pilot may be used to inform future policy.

Under this policy, Health Canada will be asking sponsors who file a new drug submission (NDS) and certain supplements to a new drug submission (SNDS) to include a pediatric development plan (PDP) with their submission. The PDP:

- should provide details of any ongoing or planned pediatric studies
- may also include a rationale for not studying the drug in all or part of the pediatric population

The policy takes effect on February 26, 2024.

All studies within the PDP will be expected to be submitted to Health Canada. Those studies, as well as any pediatric data submitted with the original NDS or SNDS, will be reviewed according to existing procedures.

Background

Many medications that are prescribed for children are prescribed off-label. Information and data from clinical trials of drugs in children are essential to support evidence-based pediatric therapies. Without this information, health care providers rely on other sources of clinical and scientific evidence to assess if the benefits of a medication outweigh the risks for a specific patient. Health Canada is taking steps to increase the availability of data that will help health care providers make these important decisions.

International regulators such as the United States Food and Drug Administration (US FDA) and the European Medicines Agency (EMA) have developed legislative and regulatory tools to encourage the:

- study of the safety and efficacy of drugs in pediatric populations and
- submission of findings from those studies to the regulatory agencies

To increase access to safety, efficacy and quality information in pediatric populations and to align with international standards, Health Canada is conducting a pilot of the pediatric study submission policy.

Scope and application

This guidance document applies to certain classes of "drugs", as defined by section 2 of the *Food and Drugs Act* (act), for human use. It includes the following products:

- pharmaceutical drugs
    - includes prescription and non-prescription pharmaceutical drugs
- biologic drugs as set out in Schedule D of the act

    - includes biotechnology products, vaccines and fractionated blood products
- radiopharmaceutical drugs as set out in Schedule C of the act

The following products are out of scope for this guidance document:

- disinfectants
- medical devices
- natural health products
- biosimilar biologic drugs
- generic pharmaceutical drugs
    - includes prescription and non-prescription pharmaceutical drugs, as well as radiopharmaceuticals

The following submission pathways are out of scope for this guidance document:

- submissions relying on third-party data submission pathway
- submissions based on the administrative submission pathway

Of note, both pharmaceutical and biologic drugs are referred to as a "drug" throughout this guidance document, unless otherwise indicated.

This guidance document applies to submissions filed under Part C, Division 8 of the *Food and Drug Regulations* (FDR):

- NDS for pharmaceutical and biologic drugs
- SNDS for new indications, new dosage forms and new routes of administration for pharmaceutical and biologic drugs

Pediatric populations for the purposes of this policy includes individuals aged from birth to under 18 years.

Policy objectives

In line with international approaches, the objectives of the pediatric study submission policy are to:

- encourage sponsors to submit, in a timely manner, safety and efficacy information for drugs expected to be used in pediatric populations
- provide more information on the safety, efficacy and dosage of drugs used in pediatric populations to health care providers, patients and their families

Note about guidance documents in general

Guidance documents provide assistance to industry and health care professionals on how to comply with governing statutes and regulations. They also provide guidance to Health Canada staff on how mandates and objectives should be met fairly, consistently and effectively.

Guidance documents are administrative, not legal, instruments. This means that flexibility can be applied. However, to be acceptable, alternate approaches to the principles and practices described in this document must be supported by adequate justification. They should be discussed in advance with the relevant program area to avoid the possible finding that applicable statutory or regulatory requirements have not been met.

As always, Health Canada reserves the right to request information or material, or define conditions not specifically described in this document, to help us adequately assess the safety, efficacy or quality of a drug. Health Canada is committed to ensuring that such requests are justifiable and that decisions are clearly documented.

Transparency

Health Canada will continue to communicate up-to-date information about drugs for human use. The following information is available online:

- Notice of compliance (NOC) database: contains NOCs issued for drugs for human use
- Drug product database: contains information about drug identification numbers (DINs) issued for drugs for human use, including the product monograph
- Drug and Health Product Portal: contains regulatory decision summaries and summary basis of decision documents, which describe Health Canada's rationale for the approval of prescription drugs for human use
- Clinical information portal: contains the clinical information filed by sponsors to seek approval of human drugs under Division 8 of the FDR

When to submit plans and studies

Pediatric studies, data and evaluations are referred to as "pediatric studies" throughout this guidance document, unless otherwise indicated.

Sponsors are asked to include the studies with the NDS or SNDS for the adult indication if a:

- pediatric study plan has been completed or
- pediatric study package is ready for regulatory review

Current guidelines and requirements for drug submissions continue to apply as outlined in the *Food and Drug Regulations* (FDR). Assessment of the studies will be conducted based on Health Canada's established approach for assessing drug safety, efficacy and quality in a pediatric population.

For information on the data protection provisions of the FDR or on the *Patented Medicines (Notice of Compliance) Regulations*, manufacturers should consult the following guidance documents:

- Data protection under C.08.004.1 of the Food and Drug Regulations
- Patented Medicines (Notice of Compliance) Regulations

Submission of pediatric studies with an NDS or SNDS will not constitute participation in the pilot, as this will continue to follow the established process.

If the pediatric studies are incomplete when the NDS or SNDS are filed, sponsors who wish to participate in the pilot should include a pediatric development plan (PDP) with their submission. This will notify Health Canada that you intend to provide the studies at a later date.

PDPs detail the research and development that a sponsor intends to undertake to generate information that may support the authorized use of a drug in a pediatric population. The plans may involve developing a:

- pediatric formulation
- pediatric extension of an existing indication
- new pediatric indication based on the active ingredient of the drug

To participate in the pilot, pediatric studies and/or the PDP must address:

- existing and proposed indications
- new dosage forms (if applicable)
- new routes of administration (if applicable)

Sponsors may also choose to develop pediatric-specific indications based on the active ingredient of the drug. For more information, see the format and content information under the Canadian plans section of this guidance.

For more information on submitting a PDP, please refer to the following sections of this guidance:

- Plans approved by a foreign authority
- Canadian pediatric development plans

If investigation of the drug in all or part of the pediatric population may not be appropriate or practical, sponsors who wish to participate in the pilot should include a rationale in the PDP.

The rationale must:

- explain in detail why the studies will not be undertaken
- contain the type of information included in a waiver request to US FDA or EMA

For more information, please refer to the following section of this guidance:

- Rationale for not conducting studies

Sponsors may submit 1 of 2 types of PDPs to Health Canada:

1. Foreign PDP:

    - may include an agreed US FDA initial Pediatric Study Plan (iPSP) or an approved EMA Pediatric Investigation Plan (EU-PIP)
        - guidance on how to complete a U.S. FDA iPSP
        - guidance on how to complete an EMA PIP (PDF)
    - may add an optional Canadian addendum to an approved foreign plan at the discretion of the sponsor if there is additional Canadian-specific context or new relevant information for Canada to consider
    - Health Canada is not accepting pediatric plans from regulators other than the US FDA or EMA as part of the pilot
2. Canadian-specific PDP:
    - may prepare and include a Canadian-specific PDP (C-PDP) if no appropriate foreign plan is available from the US FDA or EMA

Sponsors may ask for a pre-submission meeting to discuss all aspects of their submissions, including PDPs. Health Canada can advise you on:

- the most appropriate approach to take when submitting pediatric studies and/or PDPs
- any unique circumstances that are not directly addressed in this guidance document

Health Canada encourages all NDS and SNDS applications within the scope of this guidance to participate in the policy pilot. While the pilot is taking place, we will be asking all sponsors submitting an NDS or SNDS to answer a brief survey at the time of filing, for data collection purposes. The survey will prompt sponsors to consider taking part in the pilot if their submissions are within scope.

Sponsors who choose to not participate will be asked to explain why. A decision to not participate in the pilot and the reasons given will not affect our review of their NDS or SNDS.

When filing the drug submission, sponsors are asked to specify in the note to reviewer if they are including pediatric studies or a pediatric development plan.

Documents should be submitted in the electronic common technical document (eCTD) format as follows:

Document type	eCTD module	eCTD document leaf title
Survey	1.0.7 General note to reviewer	Survey
Foreign agreed/approved PDP(s)	1.2.7 International information	FDA iPSP or EMA PIP

Document type	eCTD module	eCTD document leaf title
Canadian-specific PDP	1.0.7 General note to reviewer	Canadian-specific PDP
Canadian addendum to PDP	1.0.7 General note to reviewer	Canadian addendum to PDP

Any supporting quality, nonclinical or clinical studies should be submitted in their respective eCTD modules and be organized in accordance with the current electronic specifications in the following guidance document:

- Preparation of drug regulatory activities in Electronic Common Technical Document (eCTD) format

For more information on how to file submissions electronically:

- Filing submissions electronically

For information on the pre-submission meeting, screening process, clarification requests, filing a submission and timelines/performance standards, consult:

- The management of drug submissions and applications

Foreign-approved plans

Format and content

Both the US FDA and EMA require detailed plans for pediatric drug development programs to be submitted during the adult drug development program. The US FDA requires an iPSP and the EMA requires a EU-PIP.

Both agencies will have typically reached agreements with the sponsor on these plans by the time a sponsor files a submission with Health Canada for the same drug.

Sponsors who wish to participate in the pilot may submit any of the following documents:

- an approved EU-PIP
- an agreed iPSP pending the US FDA's final decision on deferral and/or waiver requests
- an agreed iPSP following final decisions by the US FDA on granting or denying deferral and/or waiver requests at the time of marketing application

Sponsors should include the most recently approved/agreed version of the plan. Sponsors who have both an iPSP and EU-PIP may select which plan to submit to participate in the pilot.

Health Canada will accept the submitted plan as the PDP.

Sponsors who submit an agreed iPSP for which the final US FDA decision on deferral and/or waiver requests is pending should contact Health Canada about how to submit the final decision. If Health Canada's review has been completed before the US FDA or EMA make their final decision, sponsors should consult the section Amending a foreign-approved PDP. This section provides information on how to submit the update.

Products with more than 1 indication may have more than 1 iPSP and/or EU-PIP. For these products, sponsors may choose plans from both the US FDA and EMA for the PDP, as appropriate. For example, sponsors may choose a US FDA plan for indication A and an EMA plan for indication B.

Information on how pediatric plans will be reviewed is provided in the section Verifying a foreign-approved PDP.

Canadian addendum

Sponsors may choose to complete a supplementary annex (Canadian addendum) if they have additional information that may help to clarify aspects of their foreign plan. This addendum may include details such as:

- communications between sponsors and foreign regulators, outside of confidential business information as defined in the *Food and Drugs Act* (act) that clarify the rationale for any aspects of the plan that may not be clear to Health Canada without this context
- special considerations to factors that are specific to the Canadian population (for example, genetic or extrinsic factors)
- information that reflects the authorized indication(s) in Canada for drugs where the Canadian-authorized indication varies from that of the US FDA and/or EMA
- relevant differences in the authorized and marketed therapies for the condition in Canada, compared to the therapies authorized and marketed in the jurisdiction for which the plan was developed
- other information that the sponsor believes is relevant to the Canadian context

Information should be submitted as a single Canadian addendum document.

Situations where the foreign decision may not apply

In some cases, the foreign decision may not align with Health Canada's pediatric study submission policy. These include the EMA class waiver and the US FDA orphan drug exemption.

EMA class waiver

Health Canada will not be following the same process as the EMA class waiver. Sponsors who do not have a PIP or an iPSP should follow the procedure outlined in the following section:

- Rationale for not conducting studies based on an adult-related condition that rarely or never occurs in children or is on the EMA class waiver

US FDA orphan drug exemption

The US FDA exempts drugs classified as orphan drugs from iPSP requirements. Health Canada will not be using the US FDA orphan drug exemption.

Sponsors taking part in the pilot who do not have an iPSP because their product has orphan status in the US will be asked to either:

- submit an approved EU-PIP, if they have one, **or**
- follow the procedure for submitting a C-PDP to outline ongoing or proposed studies and/or
- provide a rationale for not studying the drug in all or part of the pediatric population

Verifying a foreign-approved PDP

Health Canada will accept iPSPs agreed to by the US FDA or PIPs approved by the EMA as the PDP for the pilot. The guidance for pediatric plan content is aligned between the 3 regulators.

Verification of a foreign-approved pediatric plan will consist of confirming that the iPSP or PIP is complete and is in line with C-PDP recommended content. During the verification, Health Canada may seek clarification on parts of the plans. Once Health Canada verifies that the foreign-approved plan meets the C-PDP content recommendations, then it will become identified as the PDP without changes to the plan.

The verification period for iPSPs and EU-PIPs begins after Health Canada issues the screening acceptance letter for the submission. We will verify the information in the foreign pediatric plans at the same time we review the rest of the submission.

Verification will be done according to the performance standards of the submission for which the pediatric plan is included. For example, if a sponsor is including pediatric plan(s) with an NDS associated with a 300-day review timeline, verification of those plans will occur within the timelines established for the submission. The verification of the foreign-approved PDP will not affect the review of the submission, including timelines.

Health Canada will advise the sponsor if the foreign pediatric plan(s) does not meet the C-PDP content recommendations. The sponsor may choose to withdraw from the pilot, or submit a C-PDP in place of the foreign plan. Withdrawal from the pilot will not affect the review decision for the associated NDS or SNDS.

Health Canada will provide the outcome of the foreign pediatric plan verification when we issue our final review decision. This will be done in a letter, which will be sent out at the time of the notice of compliance (NOC). The letter will identify the timeframe within which the completed pediatric study reports should be submitted to Health Canada.

We request that all studies within the PDP be submitted within 6 months of the final study completion, unless otherwise agreed to by the sponsor and Health Canada.

If:

- the review decision on the submission is negative, no decision will be made on the foreign pediatric plan
- a drug authorized for sale in Canada is cancelled pre- or post-market, completion of the studies identified in the PDP for that drug will not be expected

Health Canada's adoption of an iPSP or EU-PIP as the Canadian PDP does not:

- indicate future concurrence with a decision by the US FDA or EMA to approve the pediatric indication, formulation or labelling change
    - We will conduct an independent review based on the Canadian context and regulatory framework.
- constitute approval of the clinical trials described in the PDP
    - Sponsors must seek approvals for clinical trials from the jurisdictions where the trials take place.

For Canadian clinical trials, sponsors should communicate with the relevant Office of Clinical Trials and follow the guidelines set out in:

- Guidance document for clinical trial sponsors: Clinical trial applications

Amending a foreign-approved PDP

Health Canada requests that sponsors inform us of all amendments once the US FDA or EMA approves them. If an iPSP or EU-PIP is amended with the foreign regulator, the approved amendment may be submitted to Health Canada in the same format in which it has been submitted to the US FDA or EMA.

Amendments should be filed through the Common Electronic Submissions Gateway (CESG) under the regulatory activity Pediatric Drug Plan – Amendments (PDPAM) in the eCTD format as follows:

Document type	eCTD module	eCTD document leaf title
Foreign amended/approved PDP(s)	1.2.7 International information	Annotated FDA iPSP Non-annotated FDA iPSP or Annotated EMA PIP Non-annotated EMA PIP

Any supporting quality, nonclinical or clinical studies should be:

- submitted in their respective eCTD modules and
- organized in accordance with the current electronic specifications in the following guidance document:

- Preparation of drug regulatory activities in Electronic Common Technical Document (eCTD) format

For more information on how to file submissions electronically, refer to:

- Filing submissions electronically

Amendments will be subject to a 10-calendar day processing period, a 15-calendar day screening period and a 90-calendar day verification service standard.

Health Canada will indicate in a letter the outcome of the amendment verification and any new submission timelines.

Canadian plans

Format and content

Sponsors who do not have an iPSP or EU-PIP can participate in the policy pilot by including a C-PDP with submissions that are within the scope of this guidance.

C-PDPs will undergo scientific review to determine whether the proposed plan is adequate to study the efficacy, safety and quality of the drug in the pediatric population(s). To be accepted into the pilot, the plan should follow the criteria outlined in this guidance. A C-PDP template is included in this guidance document.

Sponsors are encouraged to consider the needs of all pediatric populations, including neonates, where possible, when developing their C-PDP. Sponsors may also propose studying the potential therapeutic benefits of the active ingredient of the drug in the relevant pediatric population for indications that go beyond those that complement existing and proposed adult indications.

All data sources should be supported by references included with the submission. Citations can include references that appear in other submission modules.

Sponsors are encouraged to review the applicable guidelines issued by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). Foreign regulators also publish relevant guidelines that can assist when developing your pediatric plans, such as:

- S11: Nonclinical safety testing in support of development of paediatric pharmaceuticals
- E11: Addendum to ICH E11: Clinical investigation of medicinal products in the pediatric population
- Pediatric study plans: Content of and process for submitting initial pediatric study plans and amended initial pediatric study plans (US FDA)
- Pediatric investigation plans (EMA)

Submissions for drugs associated with more than 1 indication may address all indications in a single pediatric plan or in separate pediatric plans.

Title page

Sponsors should include the following information about the drug in the title page of the PDP:

- drug brand name
- drug proper or common name
- dosage form
- therapeutic, diagnostic or pharmacological classification and code
    - in accordance with the World Health Organization's Anatomical Therapeutic Chemical (ATC) index
- approved indication(s) (if applicable)
- proposed indication(s)
- key elements of proposed plan:
    - age groups for which a rationale for not conducting studies is provided
    - age groups for which studies will be undertaken
    - identification of the study types
- control numbers for any previous submissions (including amendments) for this drug relevant to the C-PDP

Overview of the disease or condition in the pediatric population

This section should briefly summarize the available information on:

- pathophysiology of the disease/condition
- incidence and prevalence in both the adult and the pediatric population
    - include information on specific age subgroups where available and/or appropriate
- method of diagnosis in both the adult and the pediatric population
- discussion of the available evidence supporting the similarities and differences between the disease/conditions in the adult and pediatric populations, as required
- currently available treatments and/or prevention strategies in the pediatric population

Sponsors may cross-reference to Module 2 of the NDS/SNDS as applicable.

Proposed pediatric development plan

In keeping with the Scope and application section of this guidance, the C-PDP should address:

- existing and proposed adult indications
- new dosage forms (if applicable)
- new routes of administration (if applicable)

If it is not appropriate or practical to investigate the drug in all or part of the pediatric population, sponsors who wish to take part in the pilot should include a rationale within the C-PDP.

The rationale should:

- explain in detail why the studies will not be undertaken
- contain the type of information included in a waiver request to the US FDA or EMA

For more information on rationales, refer to the following sections of this guidance:

- Rationale for not conducting studies
- Rationale for not conducting studies based on an adult-related condition that rarely or never occurs in children or is on the MA class waiver

A C-PDP is based on the knowledge of the drug and disease/condition at the time the NDS or SNDS is submitted to Health Canada. During the implementation of the plan, additional data may become available that may affect aspects of the C-PDP. Sponsors may submit amendments to an agreed C-PDP according to the process outlined in the section on Amending an agreed-to Canadian PDP.

Overview of planned extrapolation to specific pediatric populations

It may be appropriate to extrapolate the efficacy of a drug if the course of the disease or condition and the expected response to the product between the pediatric and adult populations are similar. In some cases, it may also be appropriate to do so from 1 pediatric age group to another.

The C-PDP should provide details on any planned extrapolation of efficacy for the proposed product.

Sponsors should also justify the use of extrapolation. This justification should include:

- information on the similarities and differences between the disease in adults and children, or between 1 pediatric age group and another, that would support the extrapolation
    - for example, disease pathogenesis, disease progression, disease characteristics
- supportive data from all available sources
    - for example, sponsor-generated data, published literature, expert panels or workshops

Extrapolation of efficacy for other drugs in the same class, if previously accepted by Health Canada, the US FDA or the EMA, may also be considered.

If appropriate, the sponsor should also discuss the:

- similarity of the efficacy-exposure-response relationships between adults and pediatrics
    - based on experience with drugs in the same class or other drugs approved for use in the same disease/disorder
- use of modelling and simulation studies to support extrapolation

In some cases, it may be possible to use existing safety and dosing information in adults or other pediatric populations to draw inferences about the safety of the drug in pediatric population(s).

Sponsors proposing to use extrapolation as a tool to support inferences about safety should clearly:

- give details on how the available knowledge of the known and/or potential safety issues in the reference population apply to the target population
- justify the use of safety extrapolations from each available source
- identify potential gaps and ensure that they are addressed elsewhere in the C-PDP, such as through clinical studies

Rationale for not conducting studies

Sponsors should provide a rationale to Health Canada when there is a reason for not conducting studies in all or part of the pediatric population.

This rationale should include:

- a summary of the supporting data for each age group for which studies will not be taking place
- supporting information from all available sources such as:
    - data from nonclinical safety assessments, findings from adult clinical trials, published literature and other applicable evidence
    - full or partial waivers previously granted to other drugs in the same class by Health Canada, the US FDA or the EMA

In line with US FDA and EMA standards for pediatric study waiver requests, this rationale should indicate that studies will not be taking place for any of the following reasons:

- The necessary studies are impossible or highly impracticable:
    - justification may be based on the incidence or prevalence of the condition in all or part of the pediatric population
- The evidence strongly suggests that the drug would be ineffective and/or unsafe in relevant pediatric populations
    - justification may be based on a pharmaceutical rationale or (preliminary) data suggesting lack of efficacy or safety in the pediatric population
    - justification may be based on the lack of efficacy in the pediatric population as a whole or in subsets, where a rationale may be provided to apply a lack of efficacy in a pediatric subset to the pediatric population as a whole
- The drug does not represent a significant therapeutic benefit over existing treatments for pediatric patients
    - justification should be based on a detailed discussion of the existing authorized and marketed treatment methods
- Rationales related to not undertaking development of pediatric formulations for specific age groups

- justification should be based on the applicant demonstrating that reasonable attempts to produce the required pediatric formulation have failed or are not feasible

Sponsors who provide a rationale for not conducting any pediatric studies are to complete only the following sections (numbering according to the C-PDP template):

- Title page
- 1 Overview of the disease or condition in the pediatric population
- 2.2 Rationale for not conducting studies
- 3 Agreements for pediatric studies with other regulatory authorities (if applicable)

Rationales for not conducting studies based on a drug being ineffective or unsafe in pediatric populations may need to be reflected in the product labelling. Appropriate labelling statements will be determined based on the data submitted and in collaboration with Health Canada.

Rationale for not conducting studies based on an adult-related condition that rarely or never occurs in children or is on the EMA class waiver

A shorter C-PDP is requested for sponsors who are unable to undertake studies on any part of the pediatric population, as the condition is on the:

- US FDA list of adult-related conditions that qualify for a waiver because they rarely or never occur in pediatrics
- EMA class waiver list

In these circumstances, sponsors should include the following in their C-PDP:

- Title page
- 2.2 Rationale for not conducting studies
  - identify the condition on the US FDA or EMA list that the product is intended to treat
  - if available, include an EMA-approved request for confirmation of the applicability of the agency's decision on class waivers
  - include a statement indicating the sponsor is unable to undertake pediatric studies

Adult cancer drugs determined to be substantially relevant to the growth or progression of a pediatric cancer

An adult cancer drug may be substantially relevant to the treatment of a different pediatric cancer. For these products, it may not be sufficient to submit a rationale for not conducting studies solely on the grounds that the condition does not occur in pediatric populations.

To develop C-PDPs for these types of drugs, sponsors are encouraged review the:

- Common commentary - EMA/FDA: Common issues requested for discussion by the respective agency concerning paediatric oncology development plans

For molecularly targeted cancer drugs, sponsors are encouraged to review the US FDA's guidance on pediatric studies of molecularly targeted oncology drugs (PDF).

The US FDA also publishes 2 regularly updated lists to support pediatric development for molecularly targeted cancer drugs:

- molecular targets that are substantially relevant to the growth and progression of pediatric cancers (PDF)
- sponsors of drugs for these molecular targets are asked to:
    - submit a C-PDP outlining the planned development program
    - explain if studies are not possible based on reasons identified in Rationale for not conducting studies in section 2 of the C-PDP
- non-relevant molecular targets that will be automatically considered for a waiver (Excel)
    - the C-PDP for these drugs should only include the:
        - Title page
        - 2.2 Rationale for not conducting studies
        - identify the molecular target
        - include a statement indicating the sponsor is providing a rationale for not conducting any pediatric studies
    - this C-PDP should not to exceed 1 page

Tabular summary of planned nonclinical and clinical development

The summary should be provided in a table that:

- lists each individual study included in the proposed C-PDP, along with each study's current status
- organizes the studies in the same order that they are discussed in their respective sections of the C-PDP
- includes any age group for which the sponsor provides a rationale for not conducting studies

The following table is an example of the recommended format for the summary table. Sponsors may use shorthand to describe the proposed studies, provided they give an explanatory note at the end of the table (for example, R = randomized, PC = placebo-controlled).

Table 1: Recommended format for study summary table (entries are examples only)

Species/age group/study ID (if known) List all groups, including those for which a rationale for not conducting studies has been provided	Type of study (if known, include dosing/treatment duration)	Comments (may include study purpose/objective)	Study status and estimated initiation/ completion date (MM/YYYY)
Nonclinical studies			
Rat Approximately PND 35 Study #: ABC123	Dose range finding juvenile toxicology 3 weeks	Study submitted with NDS application	Completed
Clinical studies			
Pediatric PK or PK/PD studies			
2 to < 12 years	Open-label, single-dose study to evaluate safety, tolerability and PK	• Results will be used to establish starting dose in confirmatory safety and efficacy study • Results will be used to extrapolate existing pop PK into the pediatric population	Estimated start: 06/2025 Estimated end: 04/2026
Clinical safety and efficacy evaluation			
0 to < 2 years	• Rationale for not conducting studies	• Studies are highly impracticable due to	n/a

Table 1: Recommended format for study summary table (entries are examples only)

Species/age group/study ID (if known) List all groups, including those for which a rationale for not conducting studies has been provided	Type of study (if known, include dosing/treatment duration)	Comments (may include study purpose/objective)	Study status and estimated initiation/ completion date (MM/YYYY)
	included in C-PDP	expected enrollment difficulty	
2 to < 12 years	• Randomized, double-blind, placebo-controlled study to investigate efficacy and safety • Treatment duration to be determined	• Assessment of safety and efficacy • Safety endpoints: adverse events, physical exams, safety lab tests • Efficacy endpoints: quality of life questionnaire, functional testing, lab testing for relevant endpoints	Enrollment not started Estimated start: 12/2026 Estimated end: 03/2029
12 to <18 years Study #: XYZ123	• Multi-centre, single-arm, open label trial to evaluate efficacy and safety of dosing	• Study submitted with NDS application	Completed

Table 1: Recommended format for study summary table (entries are examples only)

Species/age group/study ID (if known) List all groups, including those for which a rationale for not conducting studies has been provided	Type of study (if known, include dosing/treatment duration)	Comments (may include study purpose/objective)	Study status and estimated initiation/ completion date (MM/YYYY)
	regimen for adolescent population • Treatment duration 6 to 12 months		
Target date for submission to Health Canada			10/2029
n/a: not applicable PK: pharmacokinetic			

Development of age-appropriate formulation

If the current formulation of the drug is not suitable for all pediatric age groups, sponsors should explain how an age-appropriate formulation will be developed for the relevant age groups.

In this section, sponsors would provide information on the:

- proposed pharmaceutical form
  - for example, liquid, capsules, tablets, ointment
- route of administration
- strength
- formulation
- appropriateness of the formulation
  - for example, discussion of its excipients and ongoing studies in the development of the formulation

Nonclinical studies

In this section, sponsors should:

- provide a brief summary of any completed, ongoing and planned nonclinical studies that support the use of the drug in the proposed pediatric age groups

- include evidence from these studies that supports the maximum dose and duration of treatment to be used in the planned clinical studies (if applicable)

If further nonclinical studies **are not required**, the sponsor should provide a clear rationale for this conclusion.

If further nonclinical studies **are required** before starting the proposed clinical trials, sponsors should provide a brief description of study. This description would include, at a minimum:

- study type
- study objectives
- species being studied
- age of animals at start of dosing
- dosing duration
- route of administration

Clinical data to support design and/or initiation of studies in pediatric patients

In this section, sponsors should:

- provide a concise overview of any existing clinical data that has been used to support the design or initiation of pediatric studies
    - include results of clinical studies of the drugs conducted to support other indications (if applicable)
- include evidence from studies that support the dose(s) and duration of treatment in the clinical studies

Ongoing and planned pediatric studies

Pediatric pharmacokinetic or pharmacokinetic/pharmacodynamic studies

In this section, sponsors should:

- include a description of each of the ongoing and planned pediatric pharmacokinetic (PK)/pharmacodynamic (PD) studies included in the tabular study summary
    - follow the order that they appear in the tabular study summary table
- address the following design aspects for each study:
    - study type
    - study design and control
    - study objectives
    - age group and population in which the study will be conducted
    - pediatric formulation(s) to be used in the study
    - dose ranges to be used in the PK studies
    - endpoints and justification (PK parameters, PD biomarkers)

- existing or planned modelling and simulation to support dose selection and/or study design, data analysis and interpretation for planned pediatric studies, including any planned extrapolation
- planned pharmacogenomic analyses
- sample size justification

Dedicated PK studies may not be needed for every age group in a C-PDP. In some cases, it may be appropriate for a sponsor to use alternative studies, such as appropriate dose scaling from adult dosing and/or confirmatory population PK studies, in place of a dedicated PK study. Sponsors should clearly and concisely justify the extrapolation study design.

Clinical efficacy and safety studies

In this section, sponsors should:

- provide a brief outline of each ongoing and planned clinical efficacy and safety study included in the tabular summary
  - follow the order that they appear in the table
- address the following design aspects for each study:
  - study type and design
  - study objectives
  - age group and population in which the study will be conducted
  - key inclusion and exclusion criteria
  - primary and key secondary efficacy endpoints
  - timing of endpoint assessments
  - safety assessments (including timing and length of follow-up)
  - statistical approach
  - modelling and simulation to be used to optimize the design of planned pediatric studies, when applicable

A detailed statistical analysis plan is not needed for the PDP.

Agreements for pediatric studies with other regulatory authorities

Sponsors with an agreed-upon foreign pediatric development plan(s) from jurisdictions other than the US FDA and EMA should include a brief summary of the plan(s) in this section. This will help Health Canada align the C-PDP with pediatric plans of other jurisdictions (where possible).

Sponsors should include:

- a copy of the most recent agreed-to or approved version of the foreign plan
- a copy of the most recent draft of the new plan or a brief summary of the changes being made to an existing plan (if negotiations are ongoing for a new or existing plan)
- any differences between the proposed C-PDP and foreign pediatric plan

Reviewing a Canadian PDP

Health Canada reviews, consults with appropriate subject matter experts and makes decisions on all C-PDPs.

Reaching an agreement on a C-PDP is a collaborative process that may require discussion between Health Canada and the sponsor. We may:

- communicate with the sponsor if, during our review, we have questions about the pediatric plan
- request a meeting to discuss elements of the plan in order to reach an agreement

Any communications concerning pediatric plans should be appropriately documented by both stakeholders and Health Canada. The processes for documenting communications, including filing any solicited and unsolicited information during the review of a pediatric plan, are the same as those for drug submissions.

For more information, please consult the following guidance document:

- The management of drug submissions and applications

The review period for C-PDPs begins after the screening acceptance letter (SAL) is issued. Health Canada will conduct the pediatric plan review at the same time as the pre-market review. The service standard for reviewing the C-PDP is the same as the service standard of the submission that included the pediatric plan.

If the sponsor and Health Canada cannot agree on the content of the C-PDP, the sponsor may withdraw from the pilot. This will not affect our review decision for the associated NDS or SNDS.

Health Canada will provide the outcome of the assessment through a letter that will be sent at the time of the notice of compliance (NOC). The letter will identify the timeframe within which completed study reports should be submitted to us. All study reports identified in the C-PDP are expected to be submitted within 6 months after the final study has been completed, unless otherwise agreed to by the sponsor and Health Canada.

If:

- the review decision on the submission is negative, no decision will be made on the C-PDP
- a drug authorized for sale in Canada becomes cancelled pre- or post-market, completion of the studies in the C-PDP for that drug will no longer be expected

Health Canada's agreement to a C-PDP is not indicative of a future positive decision on the pediatric studies submitted as a result of the C-PDP for the purpose of obtaining approval of a pediatric indication, formulation or labelling change. We will conduct a full

and independent review of all studies included in subsequent drug submissions based on the C-PDP.

Likewise, agreement to a C-PDP does not constitute approval of the clinical trials described in the plan. Sponsors are responsible for seeking approvals for clinical trials as required by the jurisdictions in which the trials take place.

For Canadian clinical trials, sponsors should communicate with the relevant Office of Clinical Trials, in accordance with the:

- Guidance document for clinical trial sponsors: Clinical trial applications

Amending an agreed-to Canadian PDP

Circumstances may arise during the course of an investigation that require a change to a C-PDP after it has been agreed to by Health Canada. If this is the case, sponsors may request an amendment to the plan.

Examples of such situations may include:

- significant delays in study completion
  - for example, over 1 year
- changes to rationales for not conducting studies
- modifications in the types of studies being conducted

All changes to a C-PDP that are outside of the scope of an amendment should be included as part of the annual report.

Sponsors may ask for an amendment to an agreed-to C-PDP at any time. Proposed changes to the C-PDP should be communicated as early as possible to allow for their review.

Amendments should be filed through the CESG under the regulatory activity type Pediatric Drug Plan – Amendments (PDPAM) in the eCTD format as follows:

Document type	eCTD module	eCTD document leaf title
Amended Canadian-specific PDP	1.0.7 General note to reviewer	Annotated C-PDP Non-annotated C-PDP

Any supporting quality, nonclinical or clinical studies should be submitted in their respective eCTD modules and organized in accordance with the current electronic specifications in the following guidance document:

- Preparation of drug regulatory activities in Electronic Common Technical Document (eCTD) format

For more information on how to file submissions electronically, refer to:

- Filing submissions electronically

A request for an amendment should include the following:

- note to reviewer, identifying the requested change(s) and justification
  - include documentation to support the request (as appropriate)
- track changes (annotated) copy of the agreed-upon C-PDP in Word
- clean version (non-annotated) of the proposed amended C-PDP in Word

Amendments will be subject to a 10-calendar day processing period, a 15-calendar day screening period and a 90-calendar day review service standard.

Amendments to a C-PDP will not be considered agreed-upon until Health Canada notifies the sponsor that it has accepted the amendments.

Canadian PDP template

For guidance on information to include in each section, refer to the Format and content section.

- Title page
- 1. Overview of the disease or condition in the pediatric population
- 2. Proposed pediatric development plan
  - 2.1 Overview of planned extrapolation to specific pediatric populations
  - 2.2 Rationale for not conducting studies
  - 2.3 Tabular summary of planned nonclinical and clinical development
  - 2.4 Development of age-appropriate formulation
  - 2.5 Nonclinical studies
  - 2.6 Clinical data to support design and/or initiation of studies in pediatric patients
  - 2.7 Ongoing and planned pediatric studies
    - 2.7.1 Pediatric pharmacokinetic or pharmacokinetic / pharmacodynamic studies
    - 2.7.2 Clinical efficacy and safety studies
- 3. Agreements for pediatric studies with other regulatory authorities

Annual reporting

Filing annual reports

To help us track the progress of pediatric plans within the pilot, we ask that sponsors keep Health Canada up to date on the status of the studies identified in their PDPs or C-PDPs. Sponsors are asked do so by submitting an annual report. Annual reports should not contain data generated during the reporting interval.

All annual reports should be filed through the CESG under the regulatory activity Pediatric Drug Plan – Annual Report (PDPAR) in the eCTD format as follows:

Document type	eCTD module	eCTD document leaf title
Annual report for foreign-approved PDP	1.0.7 General note to reviewer	PDP annual report [date]
Annual report for C-PDP	1.0.7 General note to reviewer	C-PDP annual report [date]

For more information on how to file submissions electronically, consult:

- Preparation of drug regulatory activities in Electronic Common Technical Document (eCTD) format
- Filing submissions electronically

Sponsors should submit a single annual report for all open PDPs and C-PDPs on the anniversary date of the NOC for a drug with which the first pediatric plan was attached.

For example:

- An NDS included a PDP and an NOC for the submission was issued on January 15, 2022
- A SNDS filed later for the same product included another PDP, where an NOC for the SNDS was issued on October 23, 2024

In this example, sponsors would provide the annual reports for both PDPs together, as a single document, by the anniversary date of January 15.

Any changes to the PDP identified in an annual report will be noted by Health Canada. An approval letter will not be issued.

Substantial changes to pediatric plans should be submitted through the pediatric plan amendment process. For more information, refer to the following sections of the guidance document:

- Amending a foreign-approved PDP
- Amending an agreed-to Canadian PDP

Annual reporting for foreign and Canadian PDPs

Annual reports for both foreign-approved PDPs and agreed to C-PDPs should include:

- a note to reviewer containing:
  - identification of all current plans for the drug
  - identification of the expected plan completion date and subsequent study submission date for each current plan

        - update the expected plan completion date and subsequent study submission date based on any changes to study dates in the annual report
        - submit delays of more than 1 year as an amendment
- annual report document containing:
    - brief summaries of modifications made to each plan since the last annual report
    - reference to any approved amendments
    - indicate if Health Canada is currently reviewing any amendments
    - include other changes that did not qualify for a dedicated amendment submission
    - brief overview of the status of each of the planned nonclinical and clinical study detailed within the plan
        - format the overview as an updated tabular summary of planned nonclinical and clinical development

Sponsors should use a format similar to that in Table 2 when preparing annual reports.

Table 2. Recommended format for annual reports (entries are provided as examples only)

Section (include section of the iPSP/PIP and study ID if available)	**Modification and rationale (if applicable) (include a brief summary of modification and rationale of why modification was necessary)**	**Completion date (include expected completion date based on agreed plan, agreed amendment or prior annual report) (include revised completion date if applicable)**	**Study status (include a brief status on whether the study is not yet started, is in progress (optional details as to which stage) or has been completed)**
Nonclinical studies Study ABC	n/a	04/2022	Study completed
Request for drug-specific waiver and Planned pediatric clinical studies	Waiver for 0 to 2 age category added Phase II clinical study in patients aged 0 to 2 years removed Age-appropriate formulation not possible This change has also been submitted as an	n/a	n/a

Table 2. Recommended format for annual reports (entries are provided as examples only)

Section (include section of the iPSP/PIP and study ID if available)	Modification and rationale (if applicable) (include a brief summary of modification and rationale of why modification was necessary)	Completion date (include expected completion date based on agreed plan, agreed amendment or prior annual report) (include revised completion date if applicable)	Study status (include a brief status on whether the study is not yet started, is in progress (optional details as to which stage) or has been completed)
	amendment (include amendment reference as appropriate)		
Planned pediatric clinical studies Study XYZ	Enrollment changed from 150 to 100, with revised numbers per age groups as follows: 12 to 17 years – 50 patients 6 to 11 years – 40 patients 3 to 5 years – 10 patients It was not possible to reach enrollment goal (include 2- to 3-line explanation for why)	Expected completion date: 02/2023 Revised completion date: 06/2023	In progress
n/a: not applicable			

Plans with subsequent SNDSs

Products with existing PDPs or C-PDPs may undergo subsequent SNDS filings. These may require either updates to the existing PDP/C-PDP document or addition of new PDPs/C-PDPs to the drug file.

If the existing plan is suitable for the proposed SNDS, the sponsor may notify Health Canada that no update to the plan is required in the note to reviewer.

If an existing plan can be updated to accommodate the proposed changes(s) in the SNDS, the sponsor may modify the existing plan and include it with the SNDS.

If the changes being sought in the SNDS require a different plan, then the sponsor may submit a new plan. The new plan will be added to the drug file, with the existing PDP(s) or C-PDP(s).

When providing an updated plan or filing a new plan, the sponsor must follow the applicable pediatric plan filing procedures outlined in this guidance.

Health Canada will assess the updated or new PDP or C-PDP according to the procedures for a foreign-approved PDP or an agreed-to C-PDP (as applicable).

Sponsors should submit a single annual report for all open PDPs on the anniversary date of the notice of compliance (NOC) for the submission containing the first pediatric plan.

For more information, refer to the Annual reporting section of this guidance.

Study reports

To align with regulatory reviews of pediatric data in other jurisdictions, sponsors are asked to submit their pediatric studies according to the timelines identified in the letter issued at the time of the NOC. If the timelines have been modified through subsequent filings, Health Canada requests that sponsors submit their completed pediatric study reports according to the timelines identified in their most recent annual report.

Sponsors submitting final reports should file a SNDS according to the procedures outlined in the following guidance document:

- The management of drug submissions and applications

Contact us

For questions on **this guidance document**, please contact:

- Biologic and Radiopharmaceutical Drugs Directorate (BRDD)
  Centre for Policy, Pediatrics and International Collaboration
  Health Products and Food Branch
  Health Canada
  Email: brdd-cppic_brdd-cppci@hc-sc.gc.ca

For questions on **document submission**, please contact:

- Resource Management and Operations Directorate (RMOD)
  Health Products and Food Branch
  Health Canada
  Office of Submissions and Intellectual Property
  Email: ereview@hc-sc.gc.ca

For **other questions**, please direct your questions to the appropriate directorate in Health Canada:

- Biologic and Radiopharmaceutical Drugs Directorate (BRDD)
  Office of Regulatory Affairs
  Health Products and Food Branch
  Health Canada
  Email: brdd.ora@hc-sc.gc.ca
- Pharmaceutical Drugs Directorate (PDD)
  Health Products and Food Branch
  Health Canada
  Email: pharma_drug_enquiries-renseignements_medicaments_pharma@hc-sc.gc.ca
- Natural and Non-prescription Health Products Directorate (NNHPD)
  Health Products and Food Branch
  Health Canada
  Email: nnhpd.consultation-dpsnso@hc-sc.gc.ca
- Marketed Health Products Directorate (MHPD)
  Health Products and Food Branch
  Health Canada
  Email: mhpd-dpsc@hc-sc.gc.ca