READER'S GUIDE TO THE SUMMARY BASIS OF DECISION - DRUGS

1.0 Product and Submission Information: Basic information regarding the submission including brand name, sponsor, medicinal ingredients, strengths, dosage forms and dates of filing and authorization.

2.0 Notice of Decision: A one-page summary of the authorization of the drug including the date of authorization, method of action, a brief description of the supporting clinical studies upon which authorization was based, the indication, dosing regimen, strength, dosage form and a paragraph summarizing the drug's acceptability under the *Food and Drug Regulations*.

3.0 Scientific and Regulatory Basis for Decision: Represents the bulk of the document and provides information in support of Health Canada's decision to authorize the product on the basis of quality (chemistry and manufacturing), pre-clinical and clinical data submitted.

Quality Basis for Decision: Health Canada's assessment of chemistry and manufacturing data submitted by the sponsor. Specific details including manufacturing steps are considered proprietary (i.e. confidential) and will not be included therein.

Drug Substance: Refers to the medicinal ingredient of the formulated drug. In the Quality Basis for Decision section, readers will find information regarding Health Canada's assessment of the development and controls related to the manufacture of the medicinal ingredient including information on the references and standards, impurities, stability and the general method of manufacture of the drug substance. Any issues related to the manufacturing and/or control that were particularly difficult or integral to the final decision, will be discussed to the extent possible[1].

Drug Product: Refers to the formulated drug in its final form including all non-medicinal ingredients. Readers will find information related to Health Canada's assessment of the manufacturing process and controls related to the drug product including sterilization, stability and adventitious agents (e.g. Virus or Transmissible Spongiform Encephalopathy) evaluations. Any issues related to the manufacturing and/or control that were particularly difficult or integral to the final decision, will be discussed to the extent possible[1].

---

[1] The confidentiality of drug submissions is anchored in Canadian common law, several federal statutes and international trade obligations. Certain aspects of the submission submitted to Health Canada are excluded from disclosure under the *Access to Information Act*.

Facilities and Equipment: Information pertaining to Health Canada's assessment of the manufacturing facility and equipment used in the production of the drug substance and drug product. References to On-site Evaluations will be included as applicable.

Adventitious Agents Safety Evaluation: Conclusions derived from the review of viral evaluation studies aimed to demonstrate that the materials used in production were considered safe, and that the approaches used to test, evaluate, and eliminate the potential risks during manufacturing were suitable. If appropriate measures were found to be taken to avoid and control non-viral adventitious agents (e.g. Prions and Transmissible Spongiform Encephalopathy) during manufacture, these will be summarized and accompanied by Health Canada's assessment, where possible.

Pre-clinical/Non-clinical Basis for Decision: Health Canada's assessment of the non-human studies performed to evaluate the effects of the drugs. This will include assessments of pharmacodynamics, pharmacokinetics, toxicology and microbiology both in animal and in-vitro models (e.g. test tube and plate assays), where appropriate.

Pre-clinical Pharmacodynamics: An overview of the non-human (non-clinical) studies on the biochemical and physiological effects of the drug and the mechanism of its actions, that factored significantly into Health Canada's decision to authorize sale of the drug in Canada. This may include studies investigating the correlation of actions and effects of the drug with its chemical structure as well as the effects on its actions with other drugs.

Pre-clinical Pharmacokinetics: An overview of the non-human (non-clinical) studies investigating the fate of drugs in the body over a period of time including the processes of absorption, distribution, localization in tissues, metabolism and elimination. The overview will focus on those studies that factored significantly into Health Canada's decision to authorize sale of the drug in Canada.

Toxicology: An overview of the non-human (non-clinical) studies investigating the potential adverse effects of various drug doses on systems including reproductive systems and development, the potential of genotoxicity (potential to cause damage to DNA) and carcinogenicity (potential to cause cancer), and any other toxicological studies conducted, including those related to impurities or metabolites.

Clinical Basis for Decision: An overview of the human studies and the results of the clinical data that figured significantly into Health Canada's decision. Included are the biochemical and physiological effects of the drug (pharmacodynamics) as well as information pertaining to absorption, distribution, metabolism, elimination, and drug interactions (pharmacokinetics). The data regarding efficacy and safety are also discussed.

Clinical Efficacy: An analysis of the effectiveness of the drug (i.e. the ability to achieve the desired effect) in humans, based on clinical data studies. Descriptions of the human trials are provided.

Clinical Safety: An analysis of the overall effects of the drug in humans caused by drug exposure. Descriptions of the human trials are provided. Adverse events observed during investigational testing and post-market actions including incident reports are discussed, and precautions or contraindications are included.

4.0 Benefit/Risk Assessment and Recommendation: A summary of the overall safety and efficacy assessment of the drug including, where available, comparative information on alternate therapies (e.g. trial comparators) and the approved use of the drug. Factors affecting the risk/benefit assessment are discussed. Risks inherent with the use of the drug are described along with strategies for mitigating the risks.

5.0 Submission Milestones: A list of the steps taken within the submission process along with the date of decision.