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Health Canada Update on Pre-Market Transparency for Drugs and Devices CAPRA Dinner Meeting

Laura Johnson – Office of Planning, Performance and Review Services, Therapeutic Products Directorate

May 31, 2016 – Toronto

June 2, 2016 – Montreal

YOUR HEALTH AND SAFETY... OUR PRIORITY.

Outline

- Drivers for increased transparency
- Pre-market transparency initiatives:
  - Summary Basis of Decision (SBD)
  - Regulatory Decision Summaries (RDS)
  - Submissions Under Review (SUR) List
- Consultation: transparency initiatives
- Phase II: RDSs, SUR List
- RDS Templates
- Consultation on individual transparency documents
- Next steps

Drivers for Increased Transparency (1)

Public demanding:

- More transparency & openness, in real time
- Access to decisions
- Information about regulatory offences
- Information to make own health decisions

Mandate Letter for Minister of Health:

"We have committed to set a higher bar for openness and transparency in government. It is time to shine more light on government to ensure it remains focused on the people it serves. Government and its information should be open by default. If we want Canadians to trust their government, we need a government that trusts Canadians. It is important that we acknowledge mistakes when we make them. Canadians do not expect us to be perfect – they expect us to be honest, open, and sincere in our efforts to serve the public interest."

- Excerpt from Mandate Letter to Minister of Health, November 13, 2015

Drivers for Increased Transparency (2)

Health Canada's Regulatory Transparency and Openness Framework (RTOF)

- Launched in 2014
- Successful completion of 15 projects in first year
- 3-year Framework and Action Plan launched (2015-2018)
- Transparency here to stay

Protecting Canadians from Unsafe Drugs Act (Vanessa's Law)

Amended subsection 30(1.2) of the *Food and Drugs Act* :

> **30 (1.2)** Without limiting the power conferred by any other subsection of this section, the Governor in Council may make regulations
>
> **(b.1)** requiring the Minister to ensure that decisions with regard to the issuance, amendment, suspension and revocation of authorizations referred to in paragraph (1), and to the imposition and amendment of terms and conditions referred to in paragraph (b), along with the reasons for those decisions, are publicly available;

Summary Basis of Decision (SBD) (1)

- What is an SBD?
  - Outlines reasons for decision to authorize a product for sale, including safety, efficacy, quality and regulatory considerations
  - Aimed at informed consumers and health professionals interested in the basis for Health Canada's decisions on devices & drugs
  - Reflects information available to the regulator at time of authorization
  - Complements the Product Monograph and/or approved labelling
- Published for:
  - New drug submissions for new active substances (NAS) and subsequent entry biologics (SEB)
  - 5-7 SBDs/ year for 'novel' Class III/IV medical devices
- Post-authorization/post-licensing activity tables (PAATs/PLATs) added to Phase II SBDs for drugs/devices

Summary Basis of Decision (SBD) (2)

- SBD Process:
  - Technical writer drafts SBD from review documents, approved Product Monograph or labelling
  - Review team comments on SBD draft
  - Sponsor reviews SBD draft (15 business days)
  - SBD is translated
  - Director, DG approves SBD
  - Publication teams posts SBD on website
- PAATs/PLATs are added to SBDs as subsequent activity takes place, for example:
  - Drug is market notified
  - Subsequent submissions are approved, rejected or cancelled
  - Summary safety review is published

SBDs Published

Product line	SBDs published: Phase I[1]	SBDs published: Phase II[2]	PAAT/PLAT Updates pub'd[2,3]
Medical Devices	30	14	14
Pharmaceuticals	137	78	218
Biologics	52	37	102
TOTAL	219	129	334

[1] Phase I SBDs were published from 2005 – Jan. 2013

[2] Sept. 1, 2012 – Mar. 31, 2016

[3] PAATs/PLATs = Post-Authorization/Post-Licensing Activity Tables. Multiple PAAT/PLAT updates may be published for one Phase II SBD (average = 2.7 PAAT/PLAT updates for each SBD, range 0-15)

For more information: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/sbd-smd/index-eng.php

Regulatory Decision Summaries (RDS) (1)

- RDS: a document posted on the Health Canada website, that outlines the rationale for Health Canada's decision regarding market authorization
- Applies to prescription pharmaceuticals, biologics, and medical devices
- RDS conveys:
  - What was the purpose of the submission?
  - Why was the decision issued?
- Includes administrative/"tombstone" information
- For some decisions, an RDS & SBD will both be posted; the RDS will link to the SBD if available

Regulatory Decision Summaries (RDS) (2)

- Phase I: RDSs are posted for:
  - Positive decisions issued after April 1, 2015 for new class IV medical device applications, and new drug submissions (NDS) and supplements (SNDS) for new uses
  - Negative decisions and cancellations for NDSs for NASs accepted into review after April 1, 2015 (to align with Submissions Under Review initiative)
- Phase II: RDSs are posted for:
  - Negative decisions and cancellations for all new class IV medical device applications and all NDSs and SNDSs for new uses, accepted into review after May 1, 2016

Regulatory Decision Summaries (RDS) (3)

Drugs and Health Products

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Regulatory Decision Summary: ROSIVER

Contact: Bureau of Gastroenterology Infection and Viral Diseases

Active ingredient(s)
Ivermectin

Therapeutic area
Other Dermatological Preparations

What was the purpose of this submission?

Rosiver (ivermectin) cream 1% has been developed for the treatment of rosacea in adults. The purpose of this New Drug Submission (NDS) was to obtain market authorization for Rosiver for the treatment of inflammatory lesions of rosacea in adults 18 years of age and older.

Why was the decision issued?

Based on two pivotal, randomized, placebo-controlled Phase 3 studies, Rosiver 1% cream applied to the face once daily for 1 year or longer, has been shown to effectively treat papules and pustules in subjects with moderate to severe inflammatory rosacea. This outcome was confirmed in a Phase 3 active-controlled study where Rosiver 1% cream was shown to be statistically superior to a current standard therapy, topical metronidazole. A total of 2047 subjects were exposed to the to-be-marketed formulation and regimen.

The treatment emergent adverse event (TEAE) profile for all 10 studies performed in subjects with moderate to severe inflammatory rosacea showed that Rosiver cream 1% is

Regulatory Decision Summaries (RDS) (4)

ingredient ivermectin (for example, Stromectol, Sklice), support the safe use of Rosiver (ivermectin cream, 1%) for the proposed indication.

For more information on Health Canada's decision, please view the Summary Basis of Decision.

Decision issued

Approved; issued Notice of Compliance in accordance with the *Food and Drug Regulations*.

Date of decision

2015-04-22

Additional information

Manufacturer
Galderma Canada Inc

Drug Identification Numbers (DIN) issued
DIN 02440342

Prescription status
Rosiver is available by prescription only.

Type of submission
New Drug Submission (New Active Substance)

Date filed
2014-05-06

Control number
172733

Regulatory Decision Summaries (RDS) (5)

- RDS Process for approvals is fairly straightforward
- Pharmaceuticals:
  - RDS is auto-generated from executive summary
  - Technical writer edits RDS
  - RDS is translated
  - Director approves RDS
  - Publication teams posts RDS on website
- RDS process for medical devices is similar (auto-generation from recommendation memo)
- RDS process for biologics: no auto-generation

RDSs Published

Product line	RDSs published as of March 31, 2016
Medical Devices	52
Pharmaceuticals	52
Biologics	27
TOTAL	131

For more information: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/rds-sdr/index-eng.php

Submissions Under Review (SUR) List (1)

- SUR List is posted on Healthy Canadians website as part of Health Canada's commitment under the RTOF
- Phase I: NDSs for NASs (prescription pharmaceuticals and biologics) accepted into review after April 1, 2015
  - Includes the medicinal ingredient(s) and therapeutic area
- Phase II: all NDSs and SNDSs for new uses accepted into review after May 1, 2016
- List is updated monthly
- When a final decision is rendered or submission is cancelled:
  - Submission is removed from the list (no longer under review)
  - RDS will be published
  - SBD may be published (approved NAS or SEB)

Submissions Under Review (SUR) List (2)

Submissions Under Review List:

Medicinal Ingredient(s)	Therapeutic Area
Alectinib	Antineoplastic agents
Alvimopan	Drugs for constipation
Antihemophilic factor (recombinant), pegylated	Antihemorrhagics
Bepotastine besilate	Ophthalmologicals
Bilastine	Antihistamines for systemic use
Botulinum antitoxin serotypes A, B, C, D, E, F, G	Immune sera and immunoglobulins
Brexpiprazole	Psycholeptics

For more information: http://www.healthycanadians.gc.ca/drugs-products-medicaments-produits/authorizing-manufacturing-autorisation-fabrication/review-approvals-evaluation-approbations/submissions-under-review-presentations-cours-examen-eng.php

Consultation: transparency initiatives

- Notice released March 13, 2015: outlined Phases I and II for both the RDS and SUR List initiatives
  - Phase I of both began in April 2015
  - Planned Phase II was to begin April 2016 (now May 2016)
- After Notice was released, Assistant Deputy Minister committed to consulting externally before proceeding with planned expansion to Phase II for both initiatives
- Consultation held in January/February of 2016
- Consultation consisted of two parts: a WebEx conference and an on-line consultation

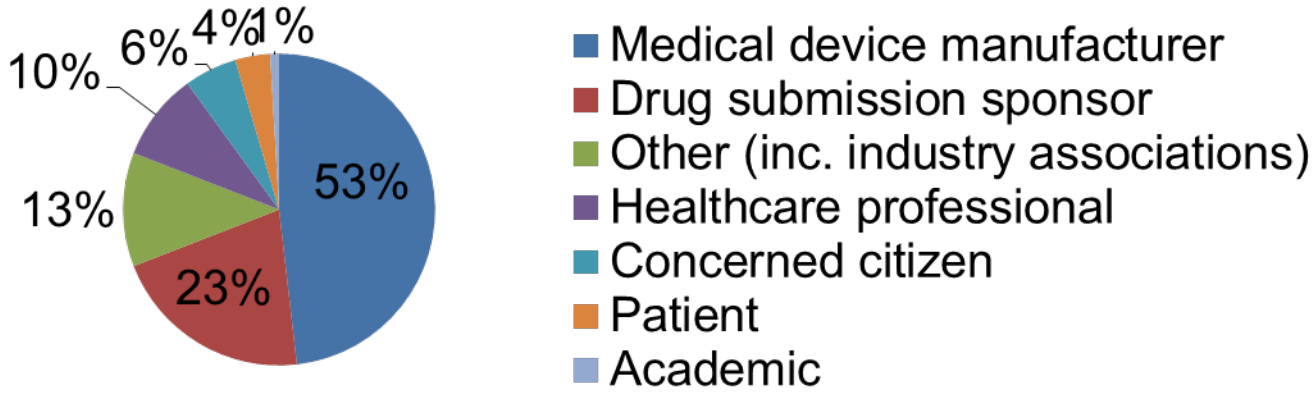
Consultation details

- External WebEx held January 27, 2016
  - 65 logged into WebEx (15 from HC)
  - 92 by phone (overlap with WebEx logins)
  - Part 1: Pre-market transparency initiatives (SBD, RDS, SUR List)
  - Part 2: Post-market transparency initiatives (Summary Safety Reviews (SSR), list of new safety reviews, list of advertising complaints)
  - Part 3: Disclosure of Confidential Business Information (CBI)

- Internal and external questionnaires available until February 19, 2016
  - 83 completed responses (external)
  - Part 1: Pre-market transparency initiatives (SBD, RDS, SUR List)
  - Part 2: Post-market transparency initiatives (SSR, list of new safety reviews, list of advertising complaints)
  - Questionnaire focused on 3 areas: awareness, utility and expansion

Respondents to the on-line questionnaire

Respondent profile: External questionnaire



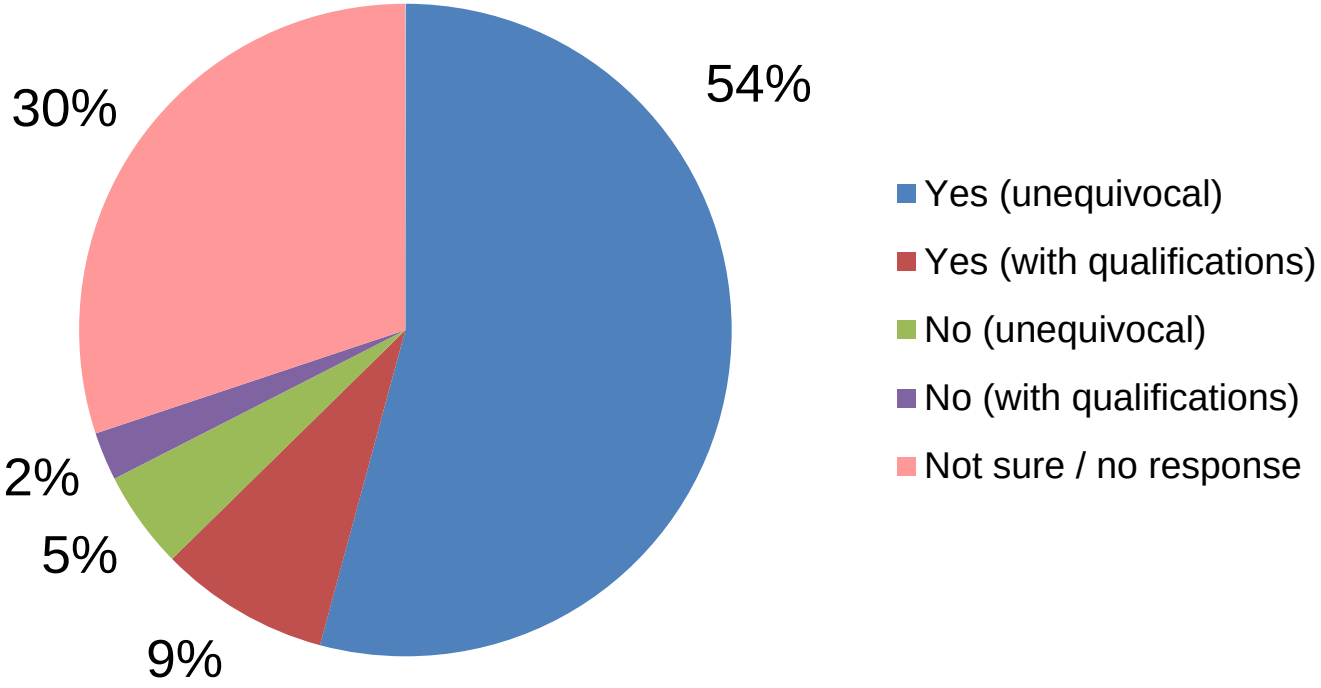
Respondent profile: Internal questionnaire

Questionnaire responses: Awareness of transparency initiatives

	Internal	External
Were you aware of SBDs?	Yes – 96% No – 4%	Yes – 61% No – 39%
Were you aware of RDSs?	Yes – 75%, No – 25%	Yes – 49% No – 51%
Were you aware of the SUR List?	Yes – 57% No – 43%	Yes – 48% No – 43%

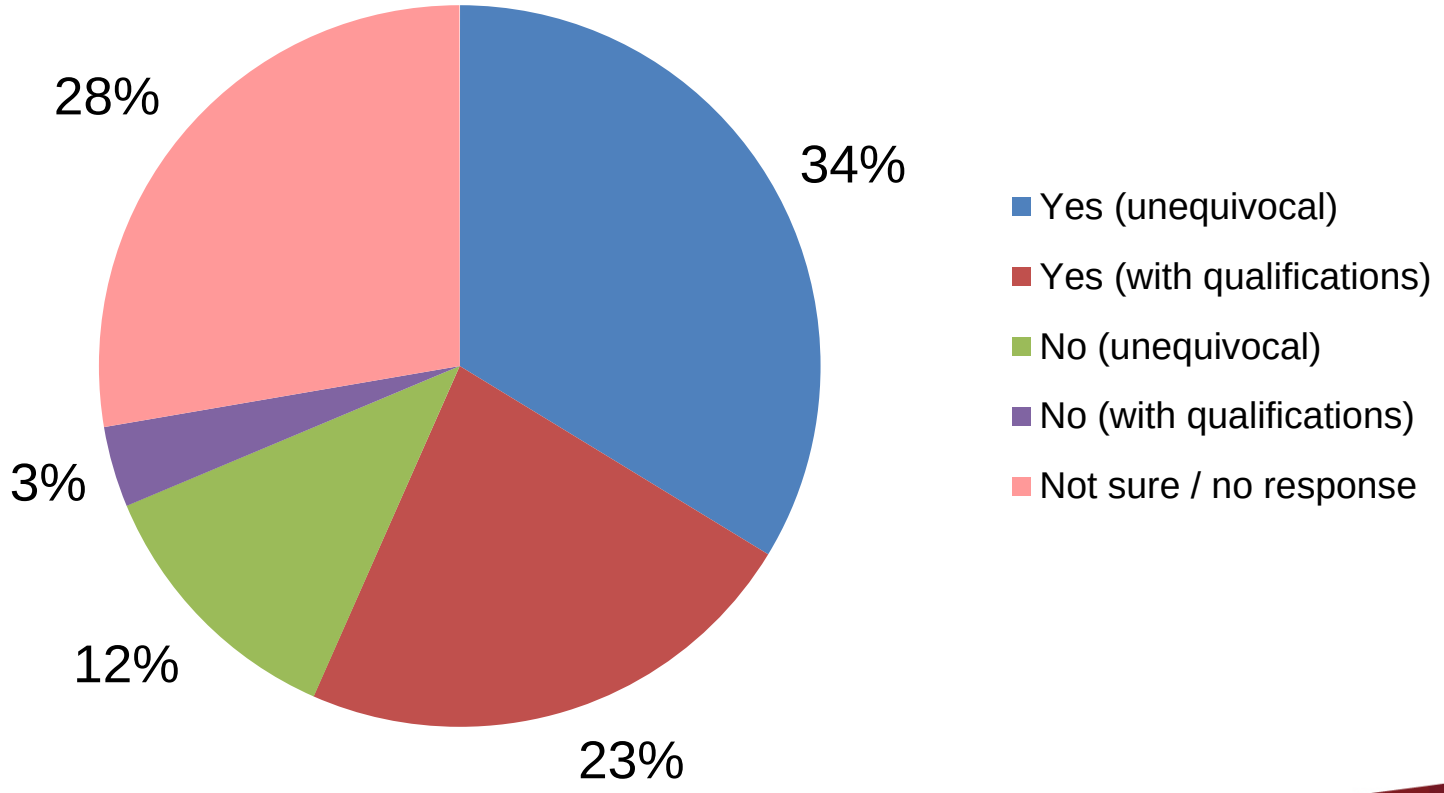
Questionnaire responses: Utility of transparency initiatives (1)

Keeping in mind other transparency and product-related information now available, are SBDs useful in understanding how HC came to a decision re: a drug or device? (External responses)



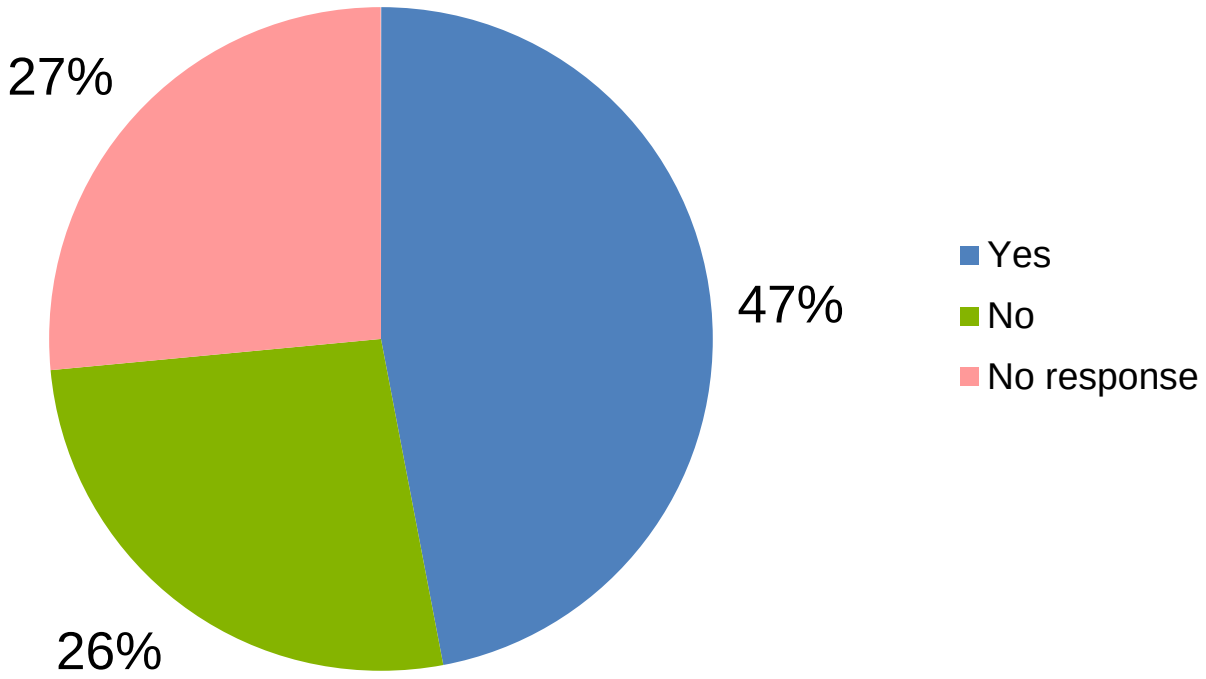
Questionnaire responses: Utility of transparency initiatives (2)

Keeping in mind other transparency and product-related information now available, are RDSs useful in understanding how HC came to a decision re: a drug or device? (External responses)



Questionnaire responses: Utility of transparency initiatives (3)

Does the SUR List provide useful information about the drug submissions HC is currently reviewing? (External responses)



Questionnaire responses: Expansion of RDSs

If we were to modify or expand RDSs….?

- Support for RDSs for additional submission types for drugs/devices already on the market
- Some support to expand to more product types (e.g. all Class III/IV devices)
- RDSs for negative decisions:
  - Strong support internally
  - Majority of drug submission sponsors not supportive
  - Medical device manufacturers more evenly split
- Concern about balancing transparency with other factors: resources, international practice, and potentially confidential information
- Information must remain understandable, retain scientific integrity
- Some suggestions re: RDS vs. SBDs and how they interrelate (to be considered as part of Phase III development)

Questionnaire responses: Expansion of SUR List

If we were to modify or expand the SUR List….?

- Support for Phase II expansion as planned
- Many respondents felt the information on the List is insufficient to be useful
- Strong support externally to include generics/SEBs (less internally)
- Strong support to include medical devices (less internally)
  - It was noted that the List is not easily transferable to medical devices in its current state
- Many suggestions for additions to the List (to be considered as part of Phase III development), including:
  - Dates (submission filed, target dates)
  - Brand names
  - Indications as submitted

Phase II: RDS and SUR List

- Announced in March 13, 2015 Notice
- Outlined in RDS, SUR List homepages
- **RDS Phase II:** Publish RDSs for negative decisions and cancellations for submissions accepted into review after **May 1, 2016**:
  - NDS
  - SNDS for new uses
  - New class IV medical device applications
- **SUR List Phase II:** Include the following on the SUR List for submissions accepted into review after **May 1, 2016**
  - NDSs
  - SNDS for new uses
- Notice posted March 18, 2016 confirming Phase II of RDS & SUR List, with a revised start date of **May 1, 2016**

Phase II: Operational Considerations

- **RDS Phase II** Operational considerations:
  - Templates for RDSs for negative decisions, cancellations
  - Timing for RDSs for negative decisions: after decision becomes final (after reconsideration/ appeal period has passed)
  - Process for RDSs for cancellations to be determined
  - Consultations with sponsors on individual RDSs for negative decisions, cancellations
- **SUR List Phase II** Operational considerations:
  - Two SUR Lists: one for NDSs, one for SNDSs
  - SNDSs: continue with therapeutic class as is (ATC 2nd level)

Current RDS Template for Drugs: approvals

- Active ingredient(s)
- Therapeutic area
- Type of submission
- Control number
- **What was the purpose of the submission?**
- **Why was the decision issued?**
- Decision issued
- Date of decision
- Additional information:
  - Manufacturer
  - DIN(s) issued
  - Prescription status
  - Date filed
- Also link to SBD if available

Proposed RDS Template for Drugs: negative decisions

**After a final decision has been issued (NOD/W or NON/W), once reconsideration period has passed*

- Active ingredient(s)
- Therapeutic area
- Type of submission
- Control number
- **What was the purpose of the submission?**
- **Why was the decision issued?**
- Decision issued
- Date of decision
- Additional information:
  - Manufacturer
  - ~~DIN(s) issued~~
  - ~~Prescription status~~
  - Date filed
- ~~Also link to SBD if available~~

Proposed RDS Template for Drugs: cancellations

**After an applicable submission has been cancelled by the sponsor, after the submission was accepted into review*

- Active ingredient(s)
- Therapeutic area
- Type of submission
- Control number
- **What was the purpose of the submission?**
- **What did the company submit to support its submission?**
- **What was the status of the submission when it was cancelled? What was HC's assessment of the submission at the time of cancellation?**
- **What consequences does the cancellation have for patients accessing the drug under SAP, or via clinical trials?**
- Date of cancellation
- Additional information:
  - Manufacturer
  - Date filed

Current RDS Template for Medical Devices: approvals

- Device class
- **What was the application for at the time of approval?**
- **What information did Health Canada review?**
- Decision issued
- Date of decision
- Additional information:
  - Manufacturer
  - Licence number issued
  - Type of application
  - Date filed
  - Application number
- Also link to SBD if available

- Templates for refusals, withdrawals are under discussion now within Medical Devices Bureau: What information to include? How to populate?

Consultation with sponsors on individual SBDs, PAATs, RDSs

- **SBDs:**
  - Currently: sponsors are consulted on each SBD (15 business days)
  - Short term proposal: continue
  - Longer term: assess as part of Phase III development
- **PAAT updates:**
  - Currently: sponsors are consulted on PAAT updates for negative decisions, cancellations (5 business days)
  - Short term proposal: send all PAAT updates for information only
- **RDSs:**
  - Currently: RDSs are not sent to sponsors for consultation
  - Short term proposal: begin sending RDSs for negative decisions, consultation to sponsors (5 business days)
  - Longer term: similar to PAATs, after gaining experience, discontinue consultation

Next Steps: SBD, RDS, SUR List

- What-was-heard report from the WebEx was published on the RTOF website in April 2016
- A summary of the consultation results on the pre-market transparency pieces will be posted online in early summer
- Over summer/fall, we will begin to consider options for Phase III of transparency initiatives, for proposed implementation spring 2017:
  - SBDs
  - RDSs
  - SUR List
  - How they interrelate
- RDSs, SBDs for drugs and devices will be incorporated into the Drug & Health Product Register in June 2016
  - Will address many consultation comments regarding single location for transparency pieces, ease of retrieval, etc.

Questions? Comments?

Laura Johnson
(613) 286-2803
laura.johnson@hc-sc.gc.ca