Accelerate CMC post approval changes

The story of a regulatory reliance pilot
Reliance: A key enabler...

...To equal access

...To timely access

...To supply continuity

Source: Good reliance practices in regulatory decision-making for medical products: WHO TRS 1033, Annex 10
Post Approval Change Vaccine Reliance Pilot

Transfer of a legacy WHO prequalified vaccine Filling & Packaging activities

37 COUNTRIES IMPACTED

FROM 4 YEARS to 6 MONTHS
Regulatory approvals x 8 time faster

Fill & Pack

Batch Release
21 countries participated in the Pilot

57% of participation
Success factors (1/2)

1 STANDARD DOSSIER
submitted in all countries
based on EU CTD dossier
content and Health Canada / WHO requirements

1 SET OF REQUIREMENTS
For all countries: some local requirements will NOT be met, based on scientific rationale

1 TIMELINE
Unique timing for all countries
after approval granted by Health Canada as the Responsible NRA

- Nov 2022
- 17 Jan 2023
- 6 months
- 17 July 2023
- 90 calendar days
- 30 cal. days
- 30 cal. days
- 30 cal. days

NRAs reviews + Questions
Sanofi answers
NRAs reviews
Approvals

17 Jan 2023
6 months
17 July 2023
90 calendar days
30 cal. days
30 cal. days
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Success factors (2/2)

1 LANGUAGE
Same language: English for all NRAs except administrative local documents

1 Q&A TOOL & DOCUMENT
1 tool & 1 Q&A document sent to all NRAs creating transparency

1 REPORT
Health Canada assessment report and Q&A shared with all NRAs as Sanofi authorises to share confidential and unredacted information

Ø GMP INSPECTION
Reliance on the GMP certificate of the French site issued routinely by ANSM

Ø TESTING
Testing considered as not necessary by Health Canada for this type of change
Key barriers encountered to engage NRAs (1/2)

**Misalignment of Reliance Principles**
- No reliance principles or principles not aligned with pilot in local regulations

**New Registration Required**
- Alternate site requires new registration

**Grace Period**
- Fixed grace period of 6/12 months after approval of dossier instead of 18 months required by Sanofi

**Documentation Requested**
- GMP documentation
- Additional Module 3 information not part of Standard Dossier
- Legalized CPP
- Extract of GMP Inspection Report
- Shipping conditions
- Dossier translated
Key barriers encountered to engage NRAs (2/2)

1 Manufacturing Site
Only 1 site authorized in the license to manufacture the vaccine

1 Batch Release Site
Only 1 site authorized in the license to release the vaccine

Sovereignty
Join the pilot only if the NRA is the reference NRA

Difficulties to connect with NRAs
NRAs not available due to Covid pandemic & outbreaks

Ressources change
New agency Director decided to leave the pilot
Transparency in the Q&A

49 QUESTIONS FROM 11 COUNTRIES

36 questions during the Q&A period from 8 countries
Approval Status & Q&A

**APPROVALS**
- 7 without questions
- 9 with questions

**% of questions asked by NRAs**
- Fewer questions: 45
- Same # questions: 30
- More questions: 25

**Questions Categories**
- Administrative: 37%
- Specifications/Analytical Procedures: 19%
- Stability: 14%
- Validation: 10%
- Labelling: 8%
- Batch Analyses: 6%
- Other: 6%
Approval Timelines (1/2)

75% of NRAs approved within 6 months (+1 month)

17 Jan 2023

90 calendar days
NRAs reviews + Questions

30 cal. days
Sanofi answers

30 cal. days
NRAs reviews

30 cal. days
Approvals

17 July 2023

6 months / 180 days

45 days
Paraguay

59 days
Saudi Arabia

69 days
El Salvador

90 days
Israel*

73 days
Europe / PEI

100 days
WHO

106 days
Jordan

146 days
Ecuador

160 days
Argentina

174 days
Chile

176 days
Thailand

182 days
Malaysia

187 days
Guatemala

188 days
Singapore

185 days
Bolivia

30 days

* Approval modules 2 & 3
Approval Timelines (2/2)

Pilot approval timeline vs maximum expected timeline

- Reliance approval timeline (calendar days)
- Maximum expected timeline (calendar days)
Local regulations and lack of global harmonization are important barriers:

- Data requirements
- Reporting levels: from limited reporting to new registration
- Inability to have alternate sites/batch release
- Timing for introduction of changes
- Perception of working outside the process
Lessons Learned (2/3)

⚠️ **Duplication of data** delaying submission
   e.g.: Legalized CPP + unredacted assessment report : 🕒 3 months

⚠️ **Site registration** requested **in parallel** of reliance variation. Sanofi did not anticipate the risk of delay.

⚠️ **Difficulties** to present the pilot
Lessons Learned (3/3)

👍 Appetite for reliance allowed 57% participation during COVID pandemic & collaboration with

👍 Openess to receive standard dossier

👍 Reduced timeline
> Faster approvals than average timeline observed
> Approval within 6 months +/-1 month
Next Steps

> Concluding on **# questions received** with/without pilot

> Collecting **feedback** of participating NRAs on pilot and Q&A tool

> **Comparing** timeline, **#questions to countries that did not participate**

> **Communication**: publication, conferences

More to come upon data analysis ...
Thank you!

sanofi