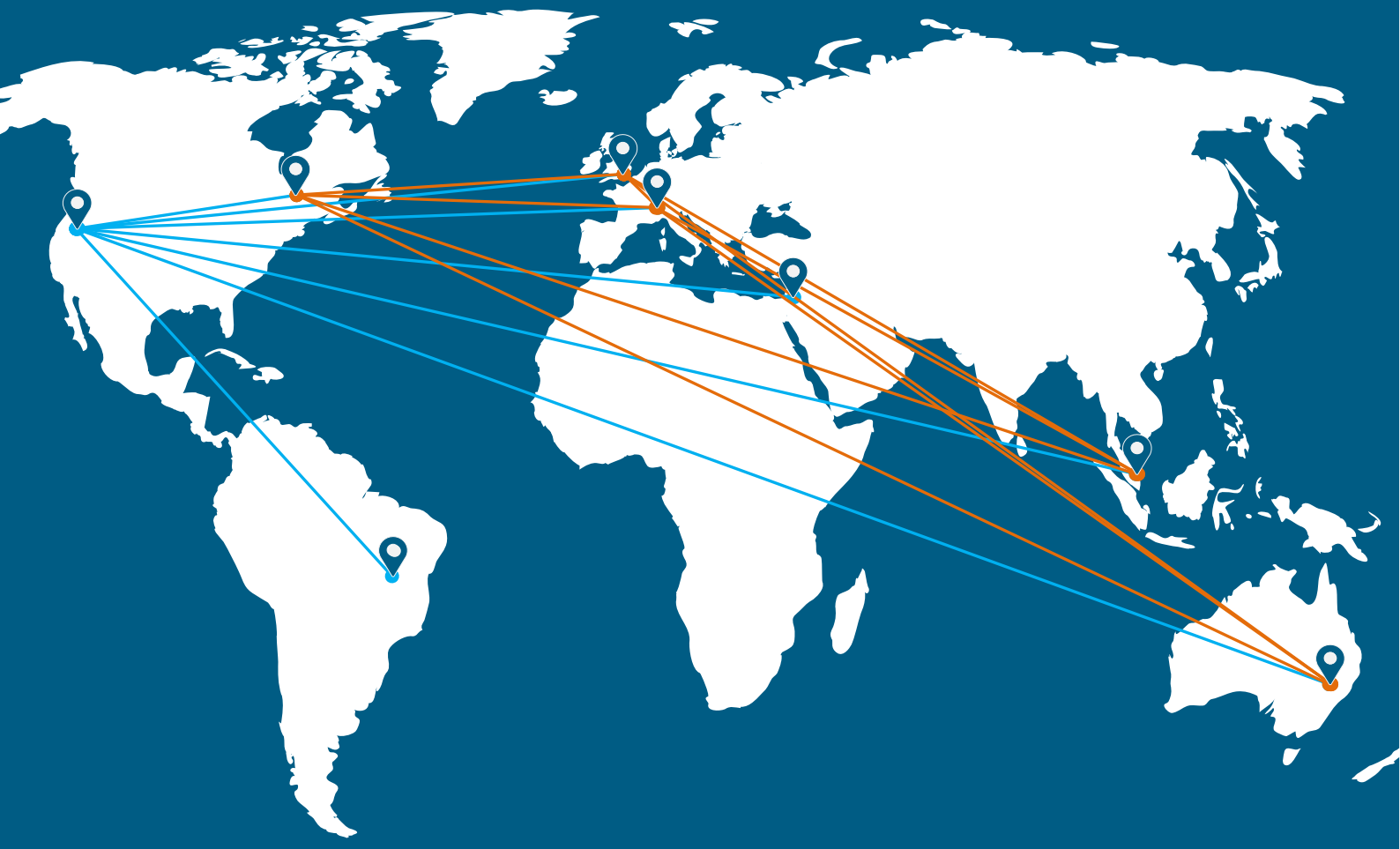
CIRS R&D Briefing 97:

Access Consortium and Project Orbis New Active Substance Approvals across Eight National Regulatory Authorities:

A five-year comparative study



CIRS Centre for Innovation in Regulatory Science

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Key messages

Access Consortium

- From 2019 to 2023, the number of new active substances (NASs) applications approved through the Access Consortium's New Active Substance Work Sharing Initiative (NASWSI) has increased. While initial approvals related to anti-cancer and immunomodulatory therapies, by 2023, approvals spanned more than ten therapeutic areas (see Figure 1).
- TGA has approved the most NASs (19) through the Access Consortium's NASWSI, followed by Swissmedic (14), Health Canada (14), HSA (10) and MHRA (3), which fully joined in 2021 (see Figure 2).
- The Access Consortium shows a considerably faster median rollout time for approved NASs than those approved via other regulatory pathways (non-Access), with a shorter median submission gap as the main driver (see Figure 4).
- NASs approved through the Access Consortium have less variable submission gaps and approval times compared to non-Access NASs (see Figures 5 and 6).

Project Orbis

- Under Project Orbis, the FDA has approved 30 NASs, followed by Health Canada (22), TGA (21), Swissmedic (13), MHRA (10), HSA (10), ANVISA (8), and the Israeli Ministry of Health (4). Notably, agencies joined Project Orbis at different times, which may have influenced these figures (see Figure 7).
- Between 2020 to 2023, the number of NASs approved through Project Orbis varied across participating authorities, as each of them showed differences in the number of approvals and the Orbis types utilised by year of approval (see Figure 8).
- NASs approved through Project Orbis have considerably faster median rollout times compared to oncology NASs that are not part of the Project Orbis process, most notably for Swissmedic, TGA and Health Canada (see Figure 9).
- NASs approved through Project Orbis Type A generally have the fastest median rollout times across all agencies, the main driver being the considerably shorter median submission gap (see Figure 10).
- NASs approved through Project Orbis have less variable submission gaps and approval times compared to non-Orbis NASs (see Figures 11 and 13).
- NASs reviewed through Project Orbis procedures are associated with higher proportions of expedited review or conditional approvals than non-Orbis NASs, contributing to faster and more consistent approval times. While Project Orbis enhances global access to therapies for severe, unmet diseases, its impact depends on each agency's regulatory framework and ability to leverage its benefits (see Figures 10, 13, 14, and 15).

Conclusion

The overall result of this study indicates that Access Consortium and Project Orbis have been effective at enhancing international collaboration and have reduced submission gaps and approval times for NASs, while expanding their therapeutic reach among participating regulatory agencies. Continuous measurement is therefore essential to refine these frameworks, address disparities, and optimise their effectiveness, ensuring they remain robust mechanisms for timely availability to innovative therapies worldwide.

About this CIRS R&D Briefing

This R&D Briefing builds upon the Centre for Innovation in Regulatory Science (CIRS)'s long-standing efforts to examine trends and practices in regulatory approvals. For over 20 years, CIRS has been conducting annual analyses of new active substance (NAS) approvals by six major regulatory agencies, providing a comprehensive view of regulatory performance over time.

These analyses have highlighted, among other facilitated regulatory pathways (FRPs), the inception and progress of the Access Consortium and Project Orbis —two prominent frameworks designed to expedite patient availability to innovative medicines by leveraging shared regulatory activities across different jurisdictions— as documented in CIRS R&D Briefings 77, 81, 85 and 93.

This briefing focuses on the Access Consortium and Project Orbis since both frameworks aim to enhance international collaboration among regulatory authorities but differ in their implementation strategies, therapeutic focus, and scope.

These differences grant an interesting opportunity to assess their impact on regulatory processes and timelines. At the same time, both models are fostering trust among stakeholders and represent a shift towards more FRPs that enable timely global approvals of innovative therapies.

The objective of this R&D Briefing is aligned with the CIRS's mission to leverage scientific principles to advance regulatory and health technology assessment (HTA) policies. Through this analysis, CIRS aims to provide insights that feed into the continuous improvement process of pharmaceutical product development, regulation, and patient access to innovative therapies. It also aims to be seen as a resource for stakeholders navigating the evolving regulatory landscape.

Data Collection and Sources

The data shown in this briefing was obtained from multiple sources to ensure comprehensive and accurate insights. Key sources included:

- **CIRS Regulatory Review Timelines Database (RRTD):** Proprietary data collected and maintained by CIRS, providing structured information on regulatory review performance for New Active Substances.
- **Publicly Available Information:** Data from regulatory agency websites, including annual reports, official announcements, and downloadable databases.
- **Direct Engagement with Regulatory Agencies:** Targeted interactions with scoped agencies to verify information, clarify regulatory processes, and supplement publicly available data.

Access Consortium

Introduction

The Access Consortium is a coalition of like-minded regulatory authorities committed to enhancing collaboration and aligning requirements to ensure timely patient access to high-quality, safe, and effective medicines.

Established in 2007 by the Therapeutic Goods Administration (TGA), Health Canada (HC), Swissmedic (SM) and the Health Sciences Authority (HSA), the consortium has launched multiple initiatives, including (but not limited to) the development of a work-sharing authorisation procedure called the New Active Substance Work-Sharing Initiative (NASWSI) back in 2018. In 2021, the Medicines and Healthcare products Regulatory Agency (MHRA) joined as a full member and has since actively contributed to NASWSI efforts.

The NASWSI facilitates the review and approval of NASs through a work-shared review process. Each agency independently evaluates Modules 1 and 2, while Modules 3 to 5 (in Common Technical Document format) are distributed among the agencies for review. Following the reviews, agencies prepare assessment reports (ARs) and lists of questions (LoQs). Other participating agencies conduct a peer review to produce, in most cases, a consolidated LoQ, which includes common and country-specific questions for the local applicant to address.

Agencies review the applicant's responses and update their ARs accordingly. If outstanding issues remain, a second cycle is initiated. Once all outstanding common issues are addressed, the ARs are finalised, and each agency completes its national procedures to issue an individual regulatory decision.

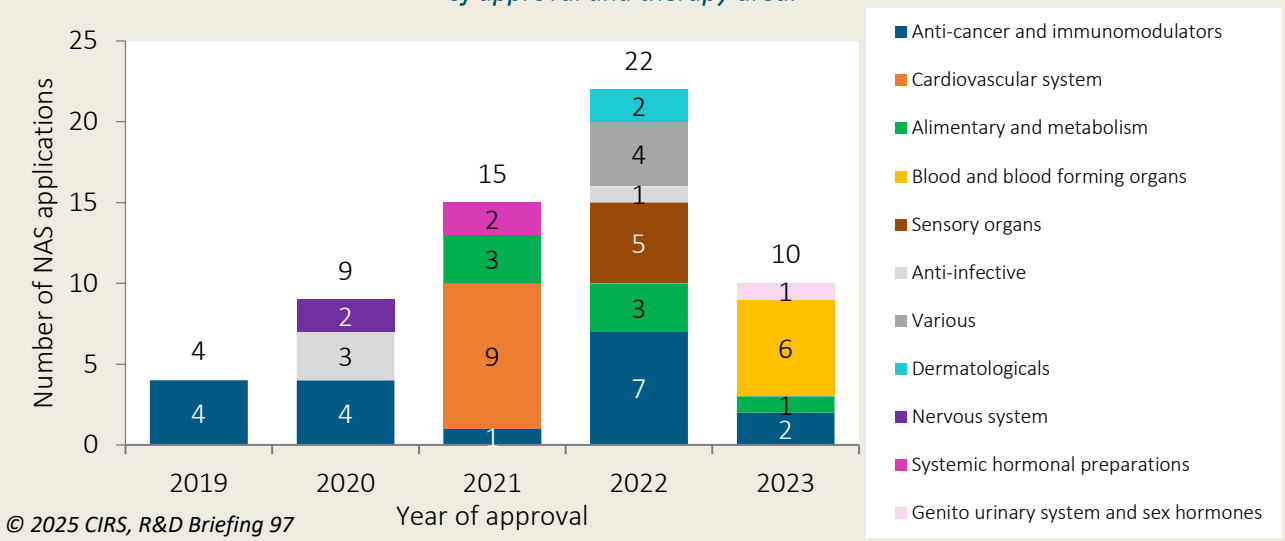
Pharmaceutical companies who have participated in the Access Consortium initiative have reported positive experiences[1], viewing it as a strategic approach to accelerating access and reducing regulatory uncertainty across multiple regions. However, this FRP faces the challenge of perceptions held by non-participating companies, as they consider the process more complex to manage than the national pathways, citing potential differences in requirements and review practices among participating agencies, which could (hypothetically) increase the risk of divergent decisions and delay approval times.

In response to these challenges and recognising the importance of NASs in therapeutic innovation, this study was undertaken to provide insights into the performance of the Access Consortium's NASWSI and to evaluate ongoing efforts.

[1] Geraci, G., Smith, R., Hansford, A. et al. Industry Perceptions and Experiences with the Access Consortium New Active Substance Work-Sharing Initiative (NASWSI): Survey Results and Recommendations. Ther Innov Regul Sci 58, 557–566 (2024). https://doi.org/10.1007/s43441-024-00624-7

NASs approved through the Access Consortium (2019–2023)

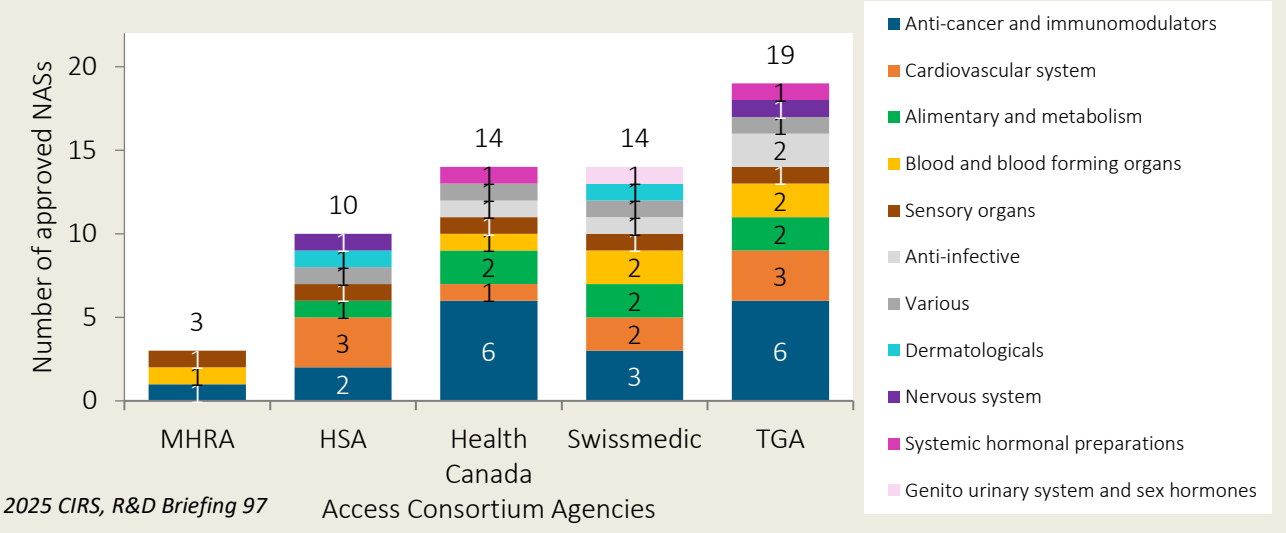
Figure 1. Number of NAS applications approved through Access Consortium (2019-2023) categorised by year of approval and therapy area.



Over the past five years, the number of NAS applications approved through the Access Consortium's NASWSI has generally increased (see Figure 1). While initial approvals were granted primarily to anti-cancer and immunomodulatory —likely reflecting the concerted efforts of industry and regulatory agencies to address unmet needs in these priority areas—by 2023, approvals spanned more than ten therapeutic areas.

More than 80% of NAS applications approved by the Access Consortium between 2019 and 2023 fall within six therapeutic areas. These include anti-cancer and immunomodulators, which account for 18 approvals (30%); cardiovascular system, with 9 (15%); alimentary and metabolism, with 7 (12%); blood and blood-forming organs, with 6 (10%); sensory organs, with 5 (8%); and anti-infective, with 4 (7%).

Figure 2. Number of approved NASs through Access Consortium (2019-2023) categorised by agency and therapy area.

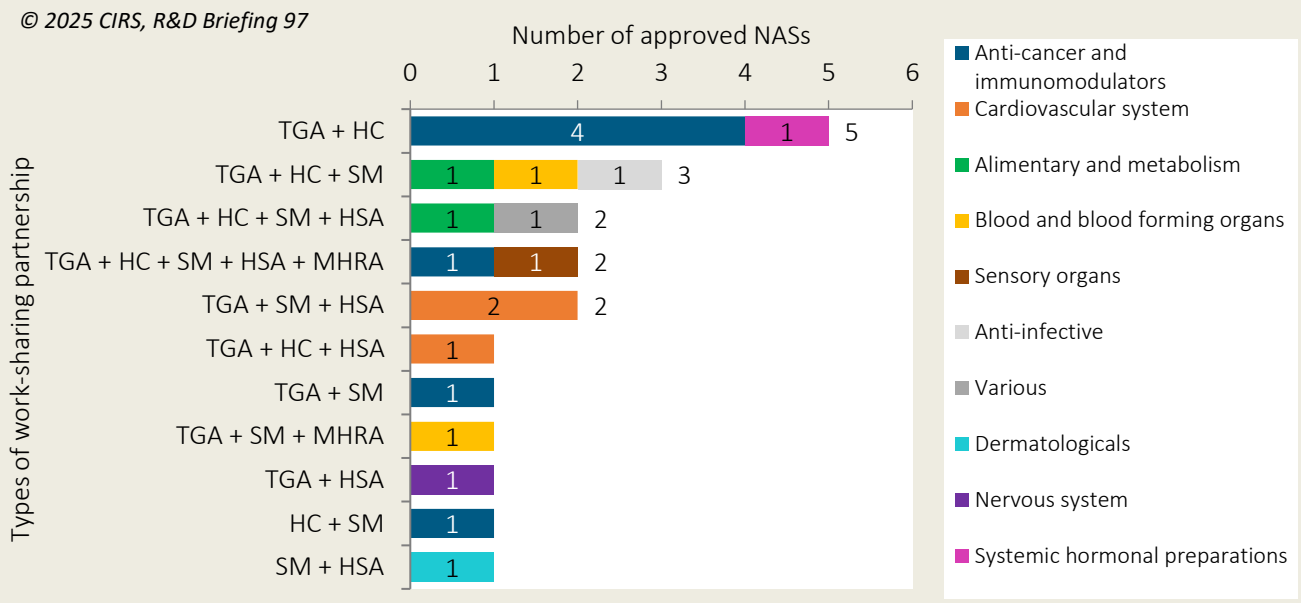


TGA has approved the highest number of NASs through the Access Consortium's NASWSI (19 in total), followed by Swissmedic (14), Health Canada (14), HSA (10) and MHRA (3), which fully joined the Consortium in 2021, (see Figure 2). Regarding therapeutic scope, Swissmedic and TGA approvals span nine different therapeutic areas, followed by Health Canada with eight and HSA with seven. The MHRA joined the Access Consortium in 2020 and began working as a full member on January 1, 2021, and approved three NASs from different therapy areas.

Work-sharing dynamics among Access Consortium agencies

An analysis of collaboration frequency among regulatory agencies from 2019 to 2023 indicates that the most common type of work-sharing partnership among specific Access Consortium members has been between TGA and Health Canada only, resulting in the approval of five NASs, four of which targeted cancer and immunological conditions (see Figure 3). The next most frequent work-sharing partnership was a tripartite between TGA, Health Canada, and Swissmedic. Other notable partnerships include TGA-HC-SM-HSA, TGA-SM-HSA, and an all-agency work-sharing collaboration, each of which resulted in two NAS approvals. The remaining six types of work-sharing partnerships were each observed at least once during the same period.

Figure 3. Number of approved NASs through Access Consortium (2019-2023) categorised by type of work-sharing partnership and therapy area.



Note: Approvals for fezolinetant, ofatumumab and molnupiravir were excluded from this analysis because, as of December 31st, 2023, only one agency had approved them as NASs.

An analysis of the number of NASs jointly approved between 2019 and 2023 highlights that TGA engaged in work-sharing activities with Health Canada 13 times, 11 times with Swissmedic, eight times with HSA, and three times with MHRA (see Table 1). Beyond joint efforts involving TGA, Swissmedic partnered with Health Canada on eight occasions, with HSA seven times, and with MHRA three times. Meanwhile, Health Canada partnered with HSA five times and MHRA three times. Finally, the HSA and MHRA worked together twice during this period.

Table 1. Number of jointly approved NASs among Access Consortium agencies.

	TGA (19)	Health Canada (14)	Swissmedic (14)	HSA (10)	MHRA (3)
TGA (19)		13	11	8	3
Health Canada (14)	13		8	5	2
Swissmedic (14)	11	8		7	3
HSA (10)	8	5	7		2
MHRA (3)	3	2	3	2	

(n) = Number of approved NASs (2019-2023)

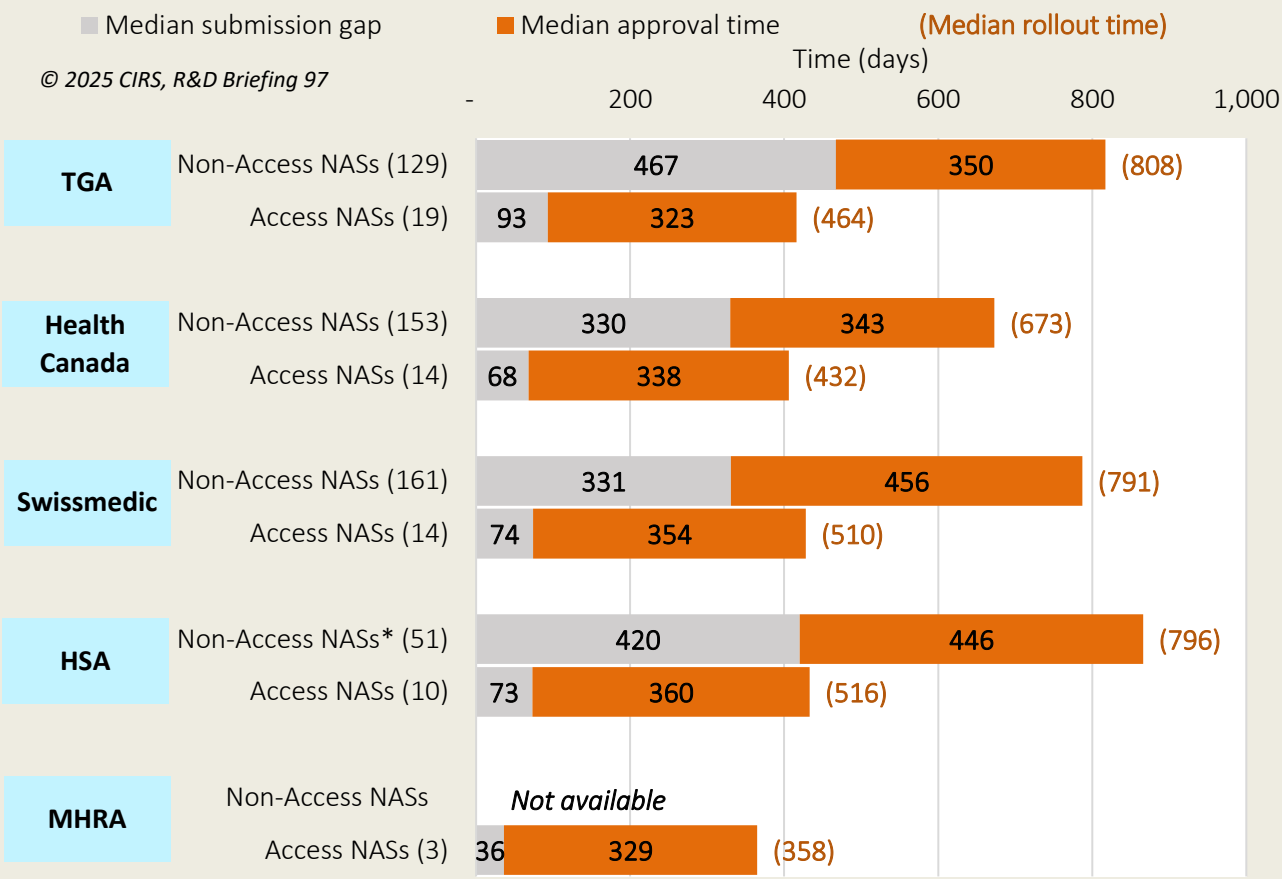
Analysis of median regulatory timelines

A comparison of regulatory timelines reveals considerably faster median rollout times for NASs approved through the Access Consortium than those approved via other regulatory pathways (see Figure 4). The greatest difference in median rollout times is observed in TGA, with a difference of 344 days between the two groups, followed by Swissmedic with 281 days, HSA with 280 days, and Health Canada with 241 days.

The primary factor driving this difference in rollout time is the shorter median submission gap for Access NASs. For instance, TGA's median submission gap for Access NASs is 93 days, 374 days shorter than for non-Access NASs (458 days). Similar trends are observed in HSA (347 days shorter), Health Canada (262 days shorter), and Swissmedic (257 days shorter).

In addition, though not across all agencies, a faster median approval time also contributes to the more rapid rollout time. Notably, Swissmedic's median approval time for Access NASs (354 days) is 102 days faster than for non-Access NASs (456 days), while HSA's median approval time for Access NASs (360 days) is 86 days faster than for non-Access NASs (446 days).

Figure 4. Comparison of median submission gap, approval time, and rollout time for NASs approved via Access Consortium vs. Non-Access NASs (2019-2023).



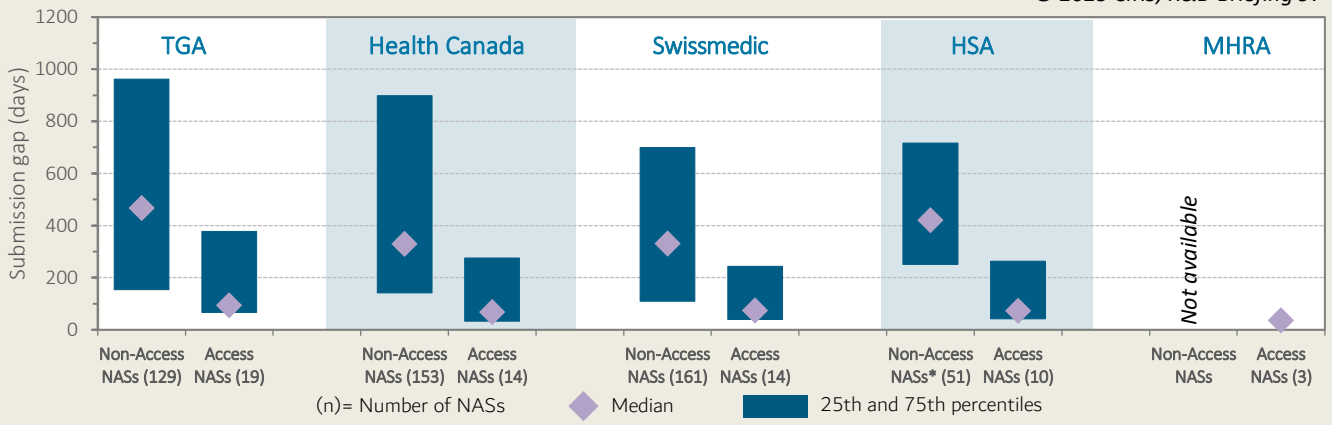
Submission gap *is calculated as the time from the date of submission at the first regulatory agency (out of EMA, FDA, PMDA, Health Canada, Swissmedic and TGA) to the date of regulatory submission to the target agency.* ***Approval time*** *is calculated from the date of submission to the date of approval by the agency. This time includes agency and company time.* ***Rollout time*** *is calculated from the date of submission at the first regulatory agency to the date of regulatory approval at the target agency.*
**The timelines for other NASs were obtained from industry via the CIRS Growth and Emerging Markets Programme.*

Analysis of variability of regulatory timelines

Submission gap variability was assessed by comparing the interquartile range (IQR; see Definitions) for Access NASs and non-Access NASs. Access NASs showed considerably less variability in submission gaps across all comparable agencies (see Figure 5). Among Access NASs, the least variable submission gap IQR was observed for Swissmedic (205 days), followed by HSA (221 days), Health Canada (242 days) and TGA (311 days).

Health Canada showed the largest difference in submission gap IQRs between Access and non-Access NASs (242 vs 757 days), followed by TGA (311 vs 808 days), Swissmedic (205 vs 589 days), and HSA (221 vs 466 days).

Figure 5. Comparison of submission gap variability of NASs approved via Access Consortium vs. Non-Access NASs (2019-2023)

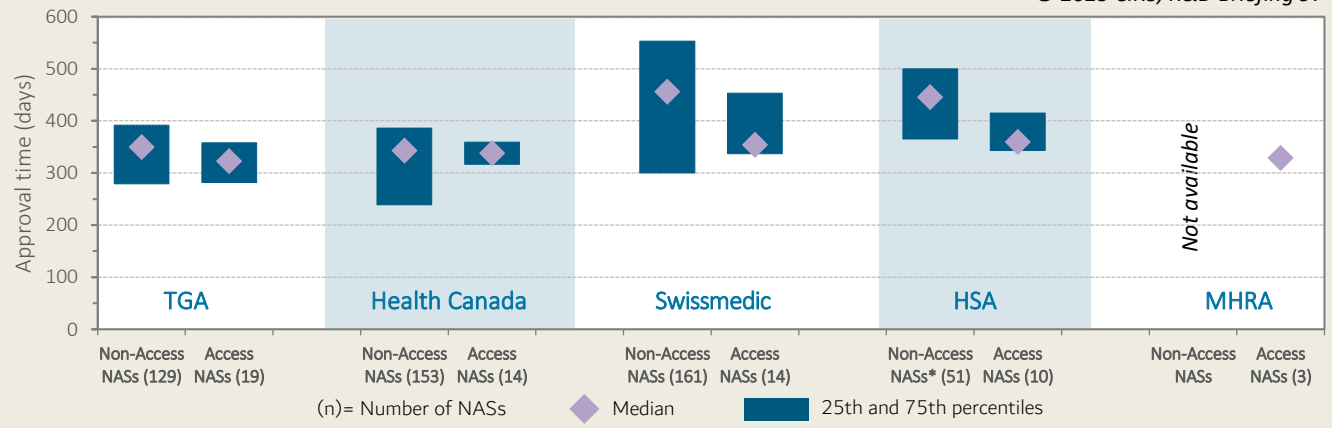


***Submission gap** is calculated as the time from the date of submission at the first regulatory agency (out of EMA, FDA, PMDA, Health Canada, Swissmedic and TGA) to the date of regulatory submission to the target agency. *The timelines for other NASs were obtained from industry via the CIRS Growth and Emerging Markets Programme.*

Approval time variability was also assessed by comparing the IQR for Access NASs and non-Access NASs. The analysis results suggest that Access NASs showed less variability in approval times across all comparable agencies (see Figure 6). Among Access NASs, the least variable approval time IQR was observed for Health Canada (42 days), followed by HSA (72 days), TGA (76 days), and Swissmedic (116 days).

Swissmedic showed the largest difference in approval time IQRs between Access NASs and non-Access NASs (116 vs 253 days), followed by Health Canada (42 vs 147 days), HSA (72 vs 135 days), and TGA (76 vs 113 days).

Figure 6. Comparison of approval time variability of NASs approved via Access Consortium vs. Non-Access NASs (2019-2023)



***Approval time** is calculated from the date of submission to the date of approval by the agency. This time includes agency and company time. *The timelines for other NASs were obtained from industry via the CIRS Growth and Emerging Markets Programme.*

Project Orbis

Introduction

Project Orbis is a global collaborative review initiative launched by the U.S. FDA's Oncology Center of Excellence (OCE) in May 2019, aimed to facilitate earlier patient access to innovative cancer therapies among participating countries where regulatory submissions might otherwise be delayed. The first wave of health authorities participating in Project Orbis included TGA and Health Canada at the initiative's inception. Swissmedic and HSA joined shortly after, in December 2019. The Brazilian Health Regulatory Agency (ANVISA) followed in May 2020, with MHRA joining in January 2021 and the Medical Technologies, Informatics, and Research Directorate at Israel's Ministry of Health (MoH of Israel) in July 2021. These health authorities form the current global partnership, and are also known as Project Orbis Partners (POPs).

Project Orbis focuses on reviewing and approving new active substances (NASs) and new indications for approved oncology drugs with impressive results or that meet high-priority review criteria, such as treating serious conditions, addressing unmet medical needs, or offering significant improvement over existing therapies. There are three collaboration levels:

- Type A, also called 'Regular Orbis', is the most collaborative process. It is initiated when an application is submitted concurrently with, or within 30 days of, the FDA submission to any POP. This process involves simultaneous submission, review with information requests —in a 'rolling questions' approach— and the possibility for (nearly) simultaneous regulatory decision-making. Key features include multi-country and application-specific meetings to address discipline-specific and overall benefit-risk topics, a mid-cycle FDA meeting and, sharing information requests.
- Type B, also called 'Modified Orbis', is initiated when an application is submitted to any POP more than 30 days after its submission to FDA. Key features include multi-country and application-specific meetings to address discipline-specific and overall benefit-risk topics and sharing information requests.
- Type C, also called 'Written Report Only Orbis', is initiated when an application is submitted to any POP any time after its submission to FDA or once FDA has completed its review. The key feature of Type C is the sharing of FDA's review documents with the POP.

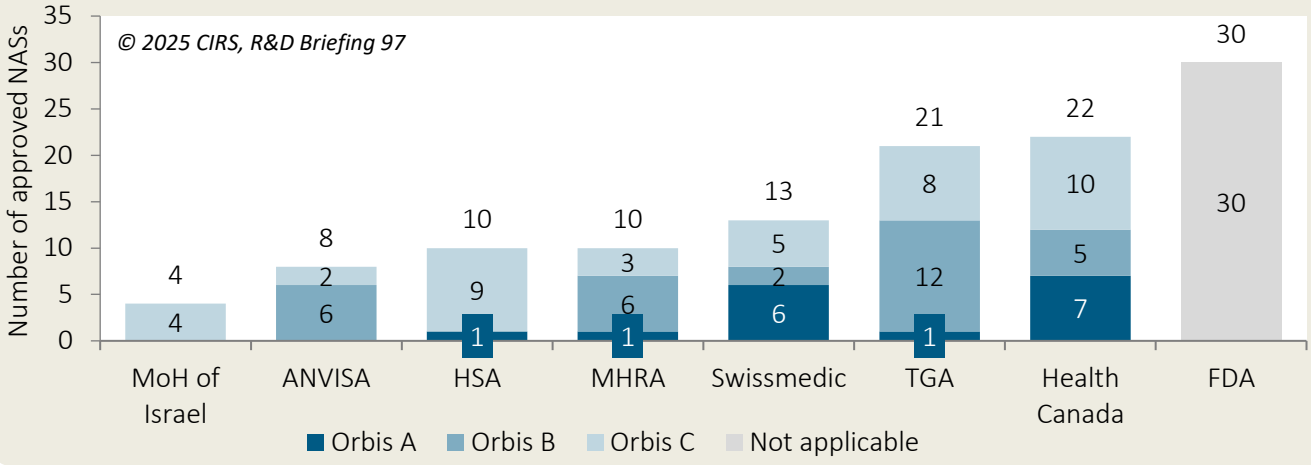
Project Orbis has been positively received by participating pharmaceutical companies as an effective pathway to expedite access to high-priority cancer treatments across multiple countries[2]. However, it presents challenges, particularly in the considerable resource demands on sponsors coordinating application submissions across jurisdictions and managing follow-ups of information requests. In addition to the challenges perceived by sponsors, agencies also face challenges like the additional workload of coordinating and facilitating meetings among POPs[3].

Recognising these complexities, CIRS analysed NASs approved through Project Orbis, aiming to provide data-driven insights into regulatory timelines and facilitate ongoing improvements in timely access to oncology innovations.

[2] Powell, S. (2024, June 18). Industry Perceptions and Experience of Orbis Projects - Survey Results and Recommendations. Presented at the DIA 2024 Global Annual Meeting, San Diego, CA, United States.
[3] de Claro, R. A., Spillman, D., Hotaki, L. T., Shum, M., Mouawad, L. S., Santos, G. M. L., Robinson, K., Hunt, M., Healy, C., Chan, A., Looi, Y. H., Rodrigues, C., Rohr, U. P., Walther, C., & Pazdur, R. (2020). Project Orbis: Global Collaborative Review Program. Clinical Cancer Research, 26(24), 6412–6416. https://doi.org/10.1158/1078-0432.CCR-20-3292

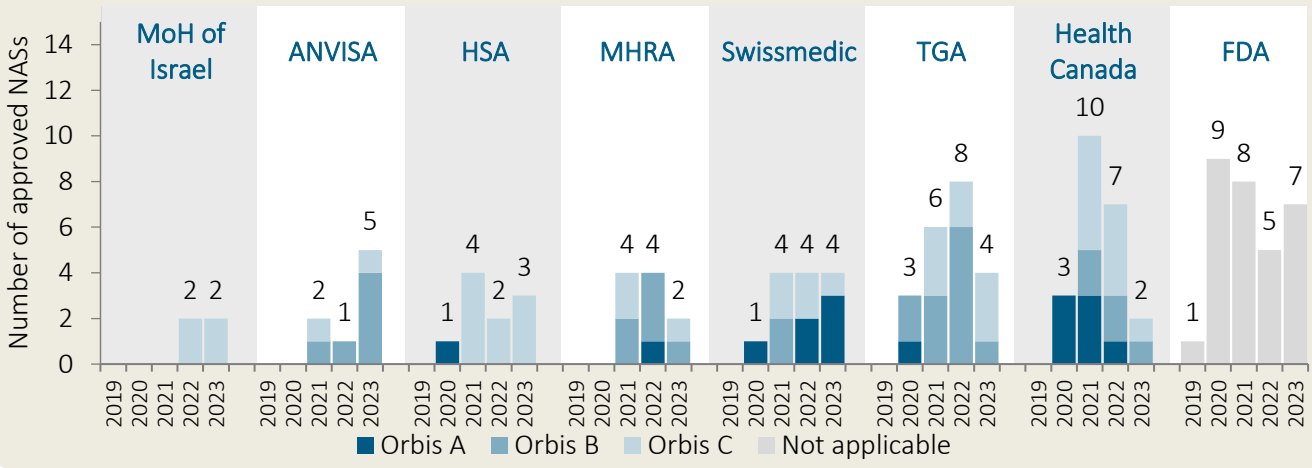
NASs approved through Project Orbis (2019–2023)

Figure 7. Number of approved NASs through Project Orbis (2019-2023) categorised by type of Orbis and agency.



Beyond the 30 NASs approved by FDA, Health Canada has approved the highest number of NASs through Project Orbis (22 NASs), followed by TGA (21), Swissmedic (13), MHRA (10), HSA (10), ANVISA (8) and the Israeli Ministry of Health (4). Notably, agencies joined Project Orbis at different times, which may influence these figures (see Figure 7). The analysis of NAS submission timing by Orbis type suggests distinct patterns across agencies driven mainly by company strategy. Health Canada had the highest number of approved NASs through Orbis A (7 of 22), followed by Swissmedic (6 of 13). In contrast, the majority of NASs were approved through Orbis B at ANVISA (6 of 8), MHRA (6 of 10), and TGA (12 of 22). Additionally, nearly all NASs were approved through Orbis C at the Ministry of Health of Israel (4 of 4) and HSA (9 of 10).

Figure 8. Number of approved NASs through Project Orbis (2019-2023) categorised by type of Orbis, year of approval and agency.



Between 2020 to 2023, the number of products approved through Project Orbis varied across participating authorities as each of them showed differences in the number of approvals and the types of Orbis utilised by year of approval (see Figure 8). In 2020, all NASs approved by early adopters like Health Canada, Swissmedic, and HSA went through Orbis A, while for TGA, 2 out of 3 NAS went through Orbis B. By 2021, the newcomers ANVISA and MHRA approved two and four NASs through a mix of Orbis B and C, respectively. Between 2022 and 2023, TGA approved 12 NASs, Health Canada nine, and both ANVISA and MHRA six each, predominantly through Orbis B and C. Swissmedic approved eight NASs during this period, five through Orbis A and the remaining three via Orbis C. Meanwhile, HSA and the Israeli Ministry of Health approved five and four NASs through Orbis C, respectively.

Analysis of median regulatory timelines

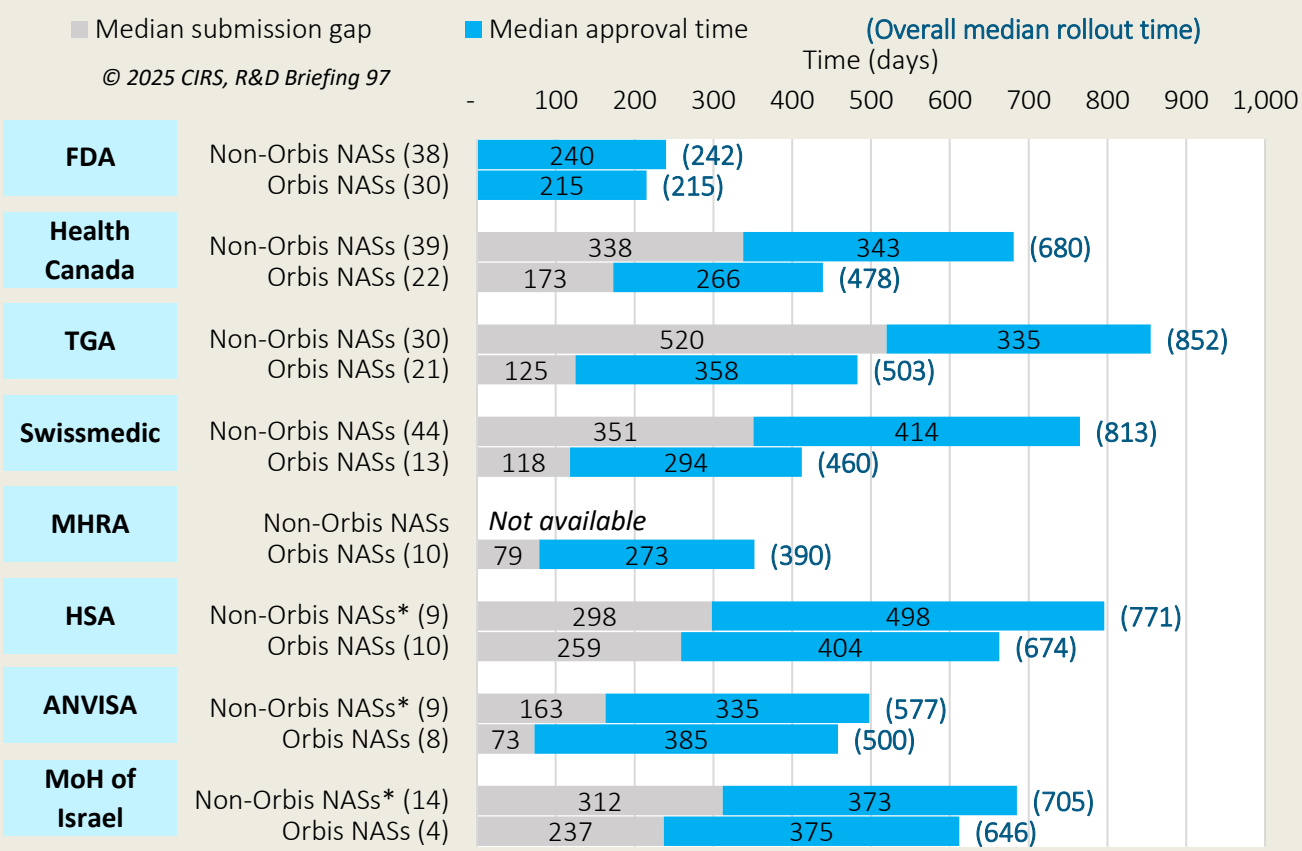
A comparison of regulatory timelines reveals considerably faster median rollout times for NASs approved through Project Orbis compared to oncology NASs that are not part of the Orbis process (non-Orbis NASs) (see Figure 9). The greatest difference in median rollout time is observed in Swissmedic, with a difference of 353 days between the two groups, followed by TGA with 349 days, Health Canada (202 days), HSA (97 days), ANVISA (77 days), the Israeli Ministry of Health (59 days), and FDA (27 days).

A key factor driving this difference in rollout time is the shorter median submission gap for Orbis NASs, though the extent of the reduction varies by agency. The most notable example is TGA, where the median submission gap for Orbis NASs is 125 days, 395 days shorter than for non-Orbis NASs (520 days). Similar trends are observed in Swissmedic (233 days shorter), Health Canada (165 days shorter), ANVISA (90 days shorter), the Israeli Ministry of Health (75 days shorter), and HSA (39 days shorter).

In addition, though not across all agencies, a faster median approval time also contribute to the more rapid rollout time. For example, Swissmedic's median approval time for Orbis NASs (294 days) is 120 days faster than for non-Orbis NASs (414 days), while HSA, Health Canada, and FDA show more modest differences of 94 days or less.

In contrast, the Israeli Ministry of Health, TGA, and ANVISA have similar median approval times for Orbis NASs than Non-Orbis NASs.

Figure 9. Comparison of median submission gap, approval time, and rollout time for NASs approved via Project Orbis vs. other non-Orbis NASs (2019-2023)



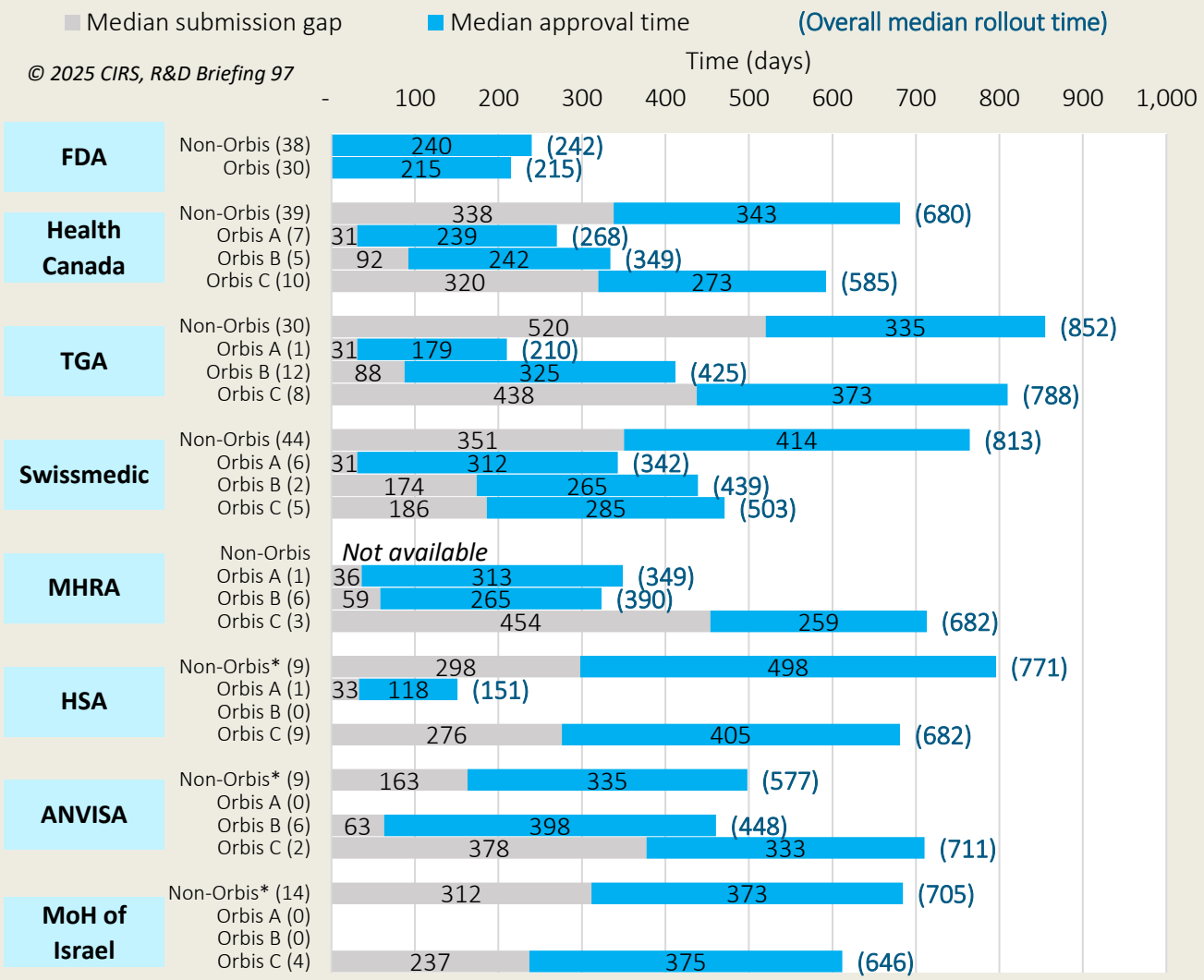
Non-Orbis NASs: *ATC L01 NASs approved outside Project Orbis. For the FDA, only those ATC L01 NASs reviewed by the OCE were considered.* ***Submission gap*** *is calculated as the time from the date of submission at the first regulatory agency (out of EMA, FDA, PMDA, Health Canada, Swissmedic and TGA) to the date of regulatory submission to the target agency. Two products were considered MLEs to FDA and NASs to other agencies within the Project Orbis, for these cases, the submission date of FDA was used instead of the date of submission at the first regulatory agency.* ***Approval time*** *is calculated from the date of submission to the date of approval by the agency. This time includes agency and company time.* ***Rollout time*** *is calculated from the date of submission at the first regulatory agency to the date of regulatory approval at the target agency.* ****:*** *The timelines for other non-Orbis NASs were obtained from industry via the CIRS Growth and Emerging Markets Programme*

A comparison of regulatory timelines by type of Orbis shows that NASs approved through Orbis A have the fastest median rollout times than those approved via Orbis B, C or non-Orbis across all agencies. The main driver for such differences is the considerably faster median submission gap (see Figure 10). For example, Health Canada, TGA, and Swissmedic report median submission gaps of 31 days followed by HSA with 33 days and MHRA with 36 days for Orbis A NASs.

Following this trend, the required minimum 30-day gap between the FDA submission date and any POP submission contributes to the longer median submission gaps observed in Orbis B NASs compared to Orbis A. These gaps range from 59 days (MHRA) to 174 days (Swissmedic). Additionally, Orbis C NASs exhibit the longest median submission gaps, ranging from 186 days (Swissmedic) to 454 days (MHRA).

Median approval times also vary across types of Orbis. Orbis A NASs have median approval times ranging from 118 days (HSA) to 313 days (MHRA), while Orbis B NASs range from 242 days (Health Canada) to 398 days (ANVISA). Additionally, Orbis C NASs have median approval times between 259 days (MHRA) and 405 days (HSA).

Figure 10. Comparison of median submission gap, approval time, and rollout time for NASs approved via Project Orbis vs. non-Orbis NASs, categorised by type of Orbis (2019-2023)



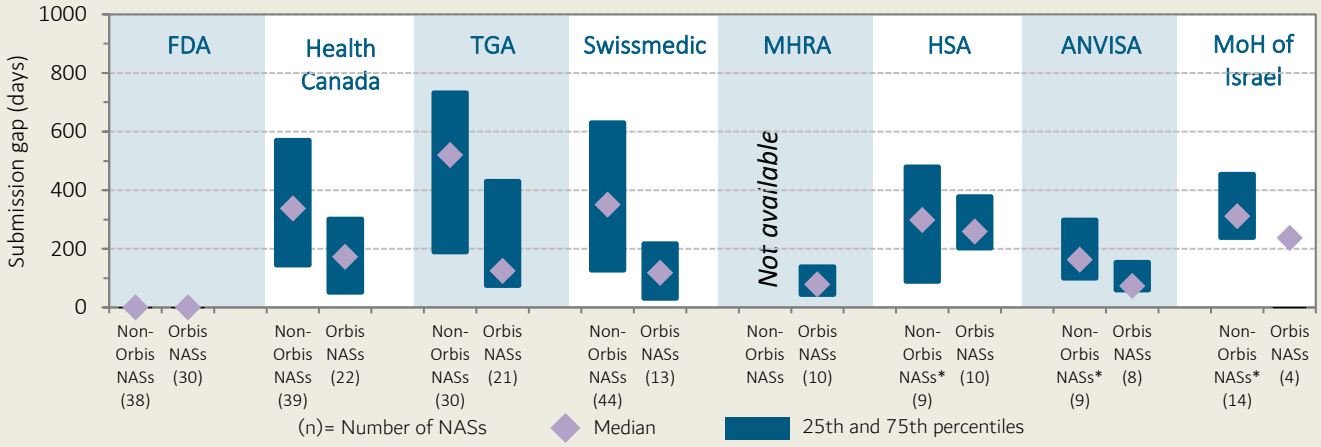
Non-Orbis NASs: *ATC L01 NASs approved outside Project Orbis. For the FDA, only those ATC L01 NASs reviewed by the OCE were considered.* ***Submission gap is*** *calculated as the time from the date of submission at the first regulatory agency (out of EMA, FDA, PMDA, Health Canada, Swissmedic and TGA) to the date of regulatory submission to the target agency. Two products were considered MLEs to FDA and considered NAS to other agencies within the Project Orbis initiative, for these cases, the FDA submission date was used instead of the date of submission at the first regulatory agency.* ***Approval time*** *is calculated from the date of submission to the date of approval by the agency. This time includes agency and company time.* ***Rollout time*** *is calculated from the date of submission at the first regulatory agency to the date of regulatory approval at the target agency.*
****:*** *The timelines for other non-Orbis NASs were obtained from industry via the CIRS Growth and Emerging Markets Programme.*

Analysis of variability of regulatory timelines

Submission gap variability was assessed by comparing the interquartile range (IQR; see Definitions) for Orbis NASs and non-Orbis NASs approved by FDA and POPs. Orbis NASs showed less variability in submission gaps across all comparable agencies (see Figure 11). Among Orbis NASs, the least variable submission gap IQRs were observed for MHRA and ANVISA (95 days), followed by HSA (176 days), Swissmedic (187 days), Health Canada (250 days), and TGA (356 days).

Swissmedic showed the largest difference in submission gap IQRs between Orbis and non-Orbis NASs (187 vs 504 days), followed by HSA (176 vs 391 days), TGA (356 vs 543 days), Health Canada (250 vs 426 days), and ANVISA (95 vs 198 days).

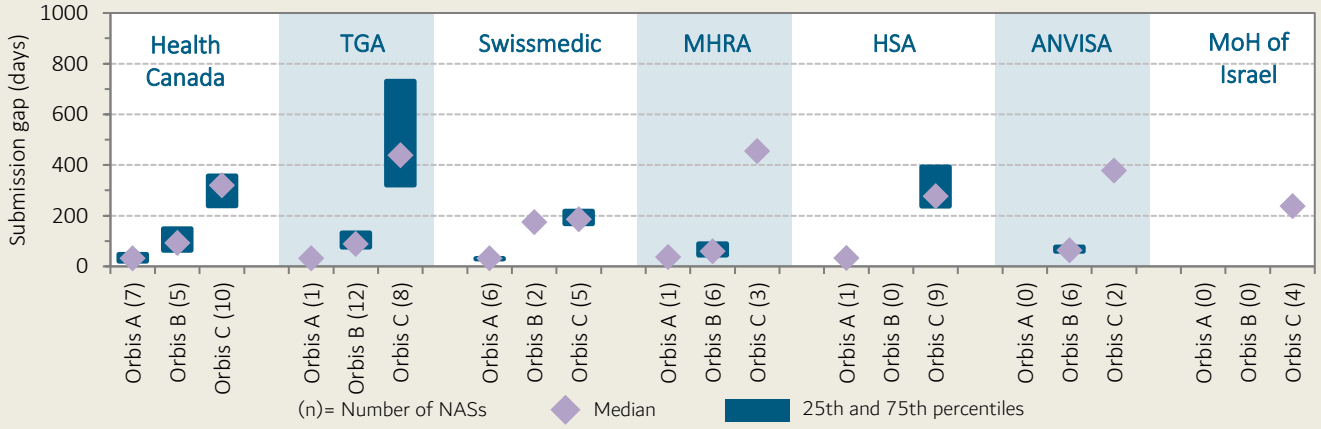
Figure 11. Comparison of submission gap variability of NASs approved via Project Orbis vs. non-Orbis NASs (2019-2023)



Non-Orbis NASs: *ATC L01 NASs approved outside Project Orbis. For the FDA, only those ATC L01 NASs reviewed by the OCE were considered.*
Submission gap *is calculated as the time from the date of submission at the first regulatory agency (out of EMA, FDA, PMDA, Health Canada, Swissmedic and TGA) to the date of regulatory submission to the target agency. Two products were considered MLEs to FDA and considered NAS to other agencies within the Project Orbis initiative, for these cases, the FDA submission date was used instead of the date of submission at the first regulatory agency. * The timelines for other non-Orbis NASs were obtained from industry via the CIRS Growth and Emerging Markets Programme.*

When categorised by type of Orbis, the analysis results suggest that Orbis A and B NASs show less variability in submission gaps than Orbis C NASs (see Figure 12). For Orbis A NASs, the submission gap IQR ranged from 2 days at Swissmedic to 28 days at Health Canada, which aligns with the expectation that Orbis A applications are submitted within 30 days of the FDA submission date. Among Orbis B NASs, ANVISA recorded the least variable submission gap IQR (18 days). In contrast, Orbis C NASs had the widest variability, with TGA showing the most variable submission gap IQR with 410 days.

Figure 12. Submission gap variability of NASs approved via Project Orbis between 2019-2023 categorised by agency and type of Orbis.

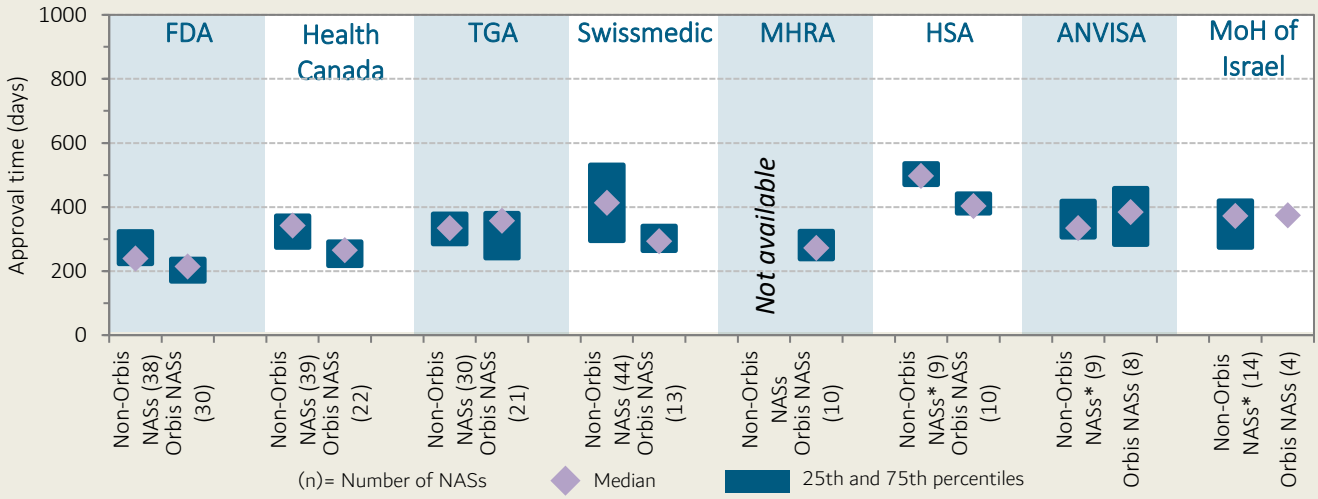


Non-Orbis NASs: *ATC L01 NASs approved outside Project Orbis. For the FDA, only those ATC L01 NASs reviewed by the OCE were considered.*
Submission gap *is calculated as the time from the date of submission at the first regulatory agency (out of EMA, FDA, PMDA, Health Canada, Swissmedic and TGA) to the date of regulatory submission to the target agency. Two products were considered MLEs to FDA and considered NAS to other agencies within the Project Orbis initiative, for these cases, the FDA submission date was used instead of the date of submission at the first regulatory agency.*

Approval time variability was also assessed by comparing the IQR for Orbis NASs and non-Orbis NASs. Orbis NASs showed less variability in approval times across all comparable agencies (see Figure 13). Among Orbis NASs, the least variable approval time IQR was observed for HSA (61 days), followed by FDA (70 days), Health Canada (75 days), Swissmedic (77 days), TGA (140 days), and ANVISA (176 days).

Swissmedic showed the largest difference in approval time IQRs between Orbis NASs and non-Orbis NASs (77 vs 237 days), followed by FDA (70 vs 101 days), Health Canada (75 vs 99 days), and HSA (61 vs 66 days). In contrast, more variable approval times for Orbis NASs than non-Orbis NASs were found in ANVISA (176 vs 113 days) and TGA (140 vs 94 days).

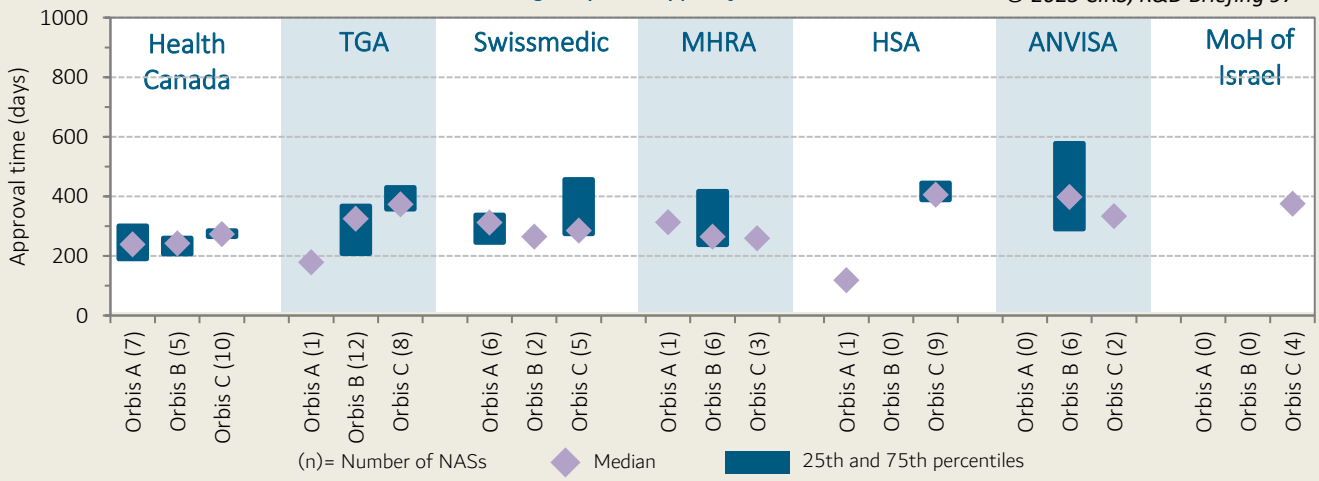
Figure 13. Comparison of approval time variability of NASs approved via Project Orbis vs. other non-Orbis NASs (2019-2023)



Non-Orbis NASs: *ATC L01 NASs approved outside Project Orbis. For the FDA, only those ATC L01 NASs reviewed by the OCE were considered.* ***Approval time*** *is calculated from the date of submission to the date of approval by the agency. This time includes agency and company time.*
****:*** *The timelines for other non-Orbis NASs were obtained from industry via the CIRS Growth and Emerging Markets Programme.*

When categorised by type of Orbis, the analysis results suggest a general trend in which Orbis A and C NASs show less variability in approval times than Orbis B NASs (see Figure 14). For Orbis C NASs, the approval time IQR ranged from 20 days for Health Canada to 183 days for Swissmedic. In comparison, for Orbis A NASs, the approval time IQR were approximately 100 days for Swissmedic and Health Canada, while Orbis B NASs had the widest variability, with ANVISA showing the most variable approval time IQR with 288 days.

Figure 14. Approval time variability of NASs approved via Project Orbis between 2019-2023 categorised by agency and type of Orbis.



Non-Orbis NASs: *ATC L01 NASs approved outside Project Orbis. For the FDA, only those ATC L01 NASs reviewed by the OCE were considered.* ***Approval time*** *is calculated from the date of submission to the date of approval by the agency. This time includes agency and company time.*

Use of expedited reviews and conditional approvals in the authorisation of NASs by four agencies

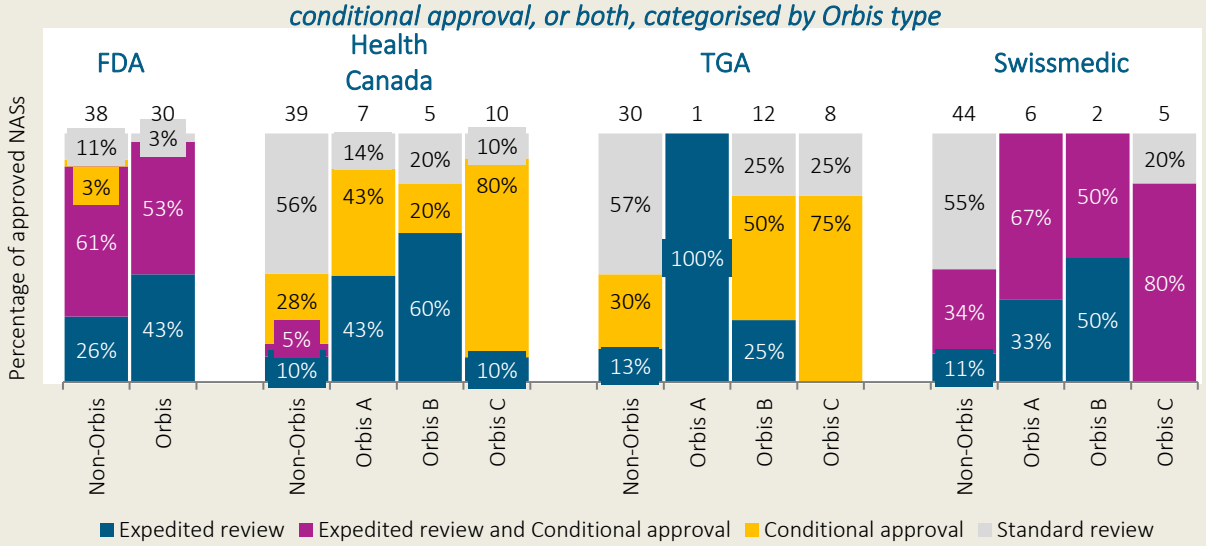
Figures 10, 13 and 14 highlight considerable differences in the median and variability of approval times between Orbis and non-Orbis NASs across TGA, Swissmedic, Health Canada, and FDA. While these differences partially reflect the impact of collaborative initiatives such as Project Orbis, they are also influenced by multiple national or agency-specific factors.

Such factors may include the severity of the condition, the size of the affected population, the availability of existing treatments, and the anticipated improvements in safety and efficacy of the therapy under review. Additionally, the availability of effective regulatory pathways that account for these considerations, along with how each agency weighs them in its decision-making process, play a crucial role in facilitating earlier patient access to innovative cancer treatments.

Such considerations influence whether a product qualifies for an expedited review or conditional approval, two regulatory processes that vary among jurisdictions and notably affect approval timelines. To better understand these dynamics, an analysis was conducted to assess the proportion of NASs reviewed through expedited processes or granted conditional approval, or both of these, across four agencies for NASs approved within and outside the Project Orbis framework.

The analysis of NAS approvals across four agencies indicates that NASs reviewed through Project Orbis are more frequently granted expedited review or conditional approval than non-Orbis NASs. This higher prevalence of facilitated regulatory pathways appears to contribute to faster and more consistent approval times. Additionally, the extent and speed to which these NASs reach different markets efficiently depends not only on the product's intrinsic characteristics but also on each agency's regulatory framework and its capacity to leverage Project Orbis' benefits (see Figures 10, 13, 14 and 15).

Figure 15. Distribution of approved NASs by four mature agencies (2019–2023) with expedited review, conditional approval, or both, categorised by Orbis type



Non-Orbis NASs: *ATC L01 NASs approved outside Project Orbis. For the FDA, only those ATC L01 NASs reviewed by the OCE were considered.* ***Expedited review*** *refers to 'Priority Review' for FDA, Health Canada, and TGA while for Swissmedic refers to 'Fast-track' review.* ***Conditional approval*** *refers to 'Accelerated approval' for FDA, 'Notice of Compliance with Conditions (NOC/c)' for Health Canada, 'Provisional approval' for TGA and 'Temporary authorisation' for Swissmedic.*

Conclusion

The overall result of this study indicates that Access Consortium and Project Orbis have been effective at enhancing international collaboration and have reduced submission gaps and approval times for NASs, while expanding their therapeutic reach among participating regulatory agencies. Therefore, continuous measurement is essential to refine these frameworks, address disparities, and optimise their effectiveness, ensuring they remain robust mechanisms for timely availability to innovative therapies worldwide.

Definitions

Approval time

Time calculated from the date of submission to the date of approval by the agency. This time includes agency and company time.

Conditional approval

Refers to 'Accelerated approval' for FDA, 'Notice of Compliance with Conditions (NOC/c)' for Health Canada, 'Provisional approval' for TGA and 'Temporary authorisation' for Swissmedic.

Expedited review.

Refers to 'Priority Review' for FDA, Health Canada, and TGA, while Swissmedic refers to 'Fast-track' review.

Interquartile range (IQR)

The interquartile range is a measure of statistical dispersion that represents the spread of the middle 50% of a dataset, and it is calculated as the difference between the value at the 75th percentile (Q3) and the 25th percentile (Q1) of a distribution of measurements.

New active substance (NAS)

A chemical, biological, biotechnology or radiopharmaceutical substance that has not been previously available for therapeutic use in humans and is destined to be made available as a 'prescription-only medicine', to be used for the cure, alleviation, treatment, prevention or in vivo diagnosis of diseases in humans. The term NAS also includes:

- An isomer, mixture of isomers, a complex or derivative or salt of a chemical substance previously available as a medicinal product but differing in properties with regard to safety and efficacy from that substance previously available.
- A biological or biotech substance previously available as a medicinal product but differing in molecular structure through changes to the nature of source material or manufacturing process and which will require clinical investigation.
- A radiopharmaceutical substance that is a radionuclide or a ligand not previously available as a medicinal product.
- Alternatively, the coupling mechanism linking the molecule and the radionuclide has not been previously available.

Applications that are excluded from the study:

- Vaccines.
- Biosimilars.
- Any other application where new clinical data were submitted.
- Generic applications.
- Those applications where a completely new dossier was submitted from a new company for the same indications as already approved for another company.
- Applications for a new or additional name or a name change for an existing compound (i.e., a 'cloned' application).
- Emergency use or Special authorisations derived from an emergency (e.g. COVID-19 pandemic).

Rollout time

Time calculated from the submission date at the first regulatory agency to the date of regulatory approval at the target agency.

Submission gap

Time calculated as the time from the submission date at the first regulatory agency (out of EMA, FDA, PMDA, Health Canada, Swissmedic and TGA) to the submission date at the target agency.

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The Centre for Innovation in Regulatory Science (CIRS) is a neutral, independent UK-based subsidiary of Clarivate plc. CIRS' mission is to identify and apply scientific principles for the purpose of advancing regulatory and health technology assessment (HTA) policies and processes. CIRS provides an international forum for industry, regulators, HTA and other healthcare stakeholders to meet, debate and develop regulatory and reimbursement policy. It is governed and operated by Clarivate for the sole support of its members' activities. The organisation has its own dedicated management and advisory boards, and its funding is derived from membership dues, related activities and grants.

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