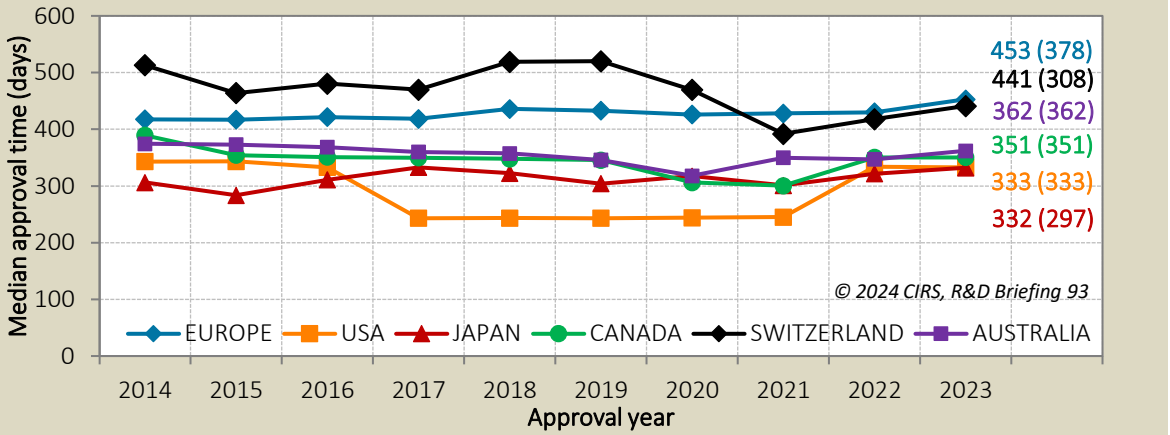
New drug approvals in six major authorities 2014-2023:

Changing regulatory landscape and facilitated regulatory pathways

This R&D Briefing presents the results from the Centre for Innovation in Regulatory Science (CIRS) annual analysis of new active substance (NAS) approvals by six major regulatory agencies: the European Medicines Agency (EMA), the US Food and Drug Administration (FDA), the Japan Pharmaceuticals and Medical Devices Agency (PMDA), Health Canada, Swissmedic and the Australian Therapeutic Goods Administration (TGA). The analysis focuses on 2023 as well as looking back at 2014-2023. Although median approval times can be a marker of agency performance and the time it takes to make medicines available to patients, other factors must be considered as illustrated in the infographic below. For example, the use of facilitated regulatory pathways (FRPs) is a major element of the submission and approval strategy and is a focus of this year's R&D Briefing.

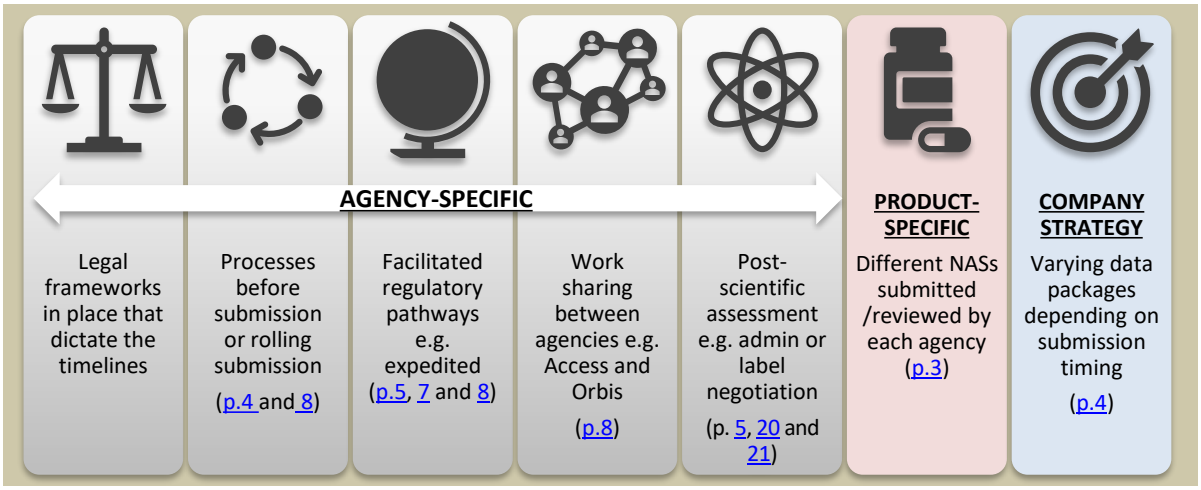
Contents

New active substance (NAS) median approval time for six regulatory authorities in 2014-2023



Approval time is calculated from the date of submission to the date of approval by the agency. This time includes agency and company time. EMA approval time includes the EU Commission time. N1 = median approval time for products approved in 2023; (N2) = median time from submission to the end of scientific assessment (see p.20) for products approved in 2023.

Differences in median time to marketing authorisation can be attributed to several factors that are agency-specific, or related to company strategy, as detailed in the infographic below.



Key messages

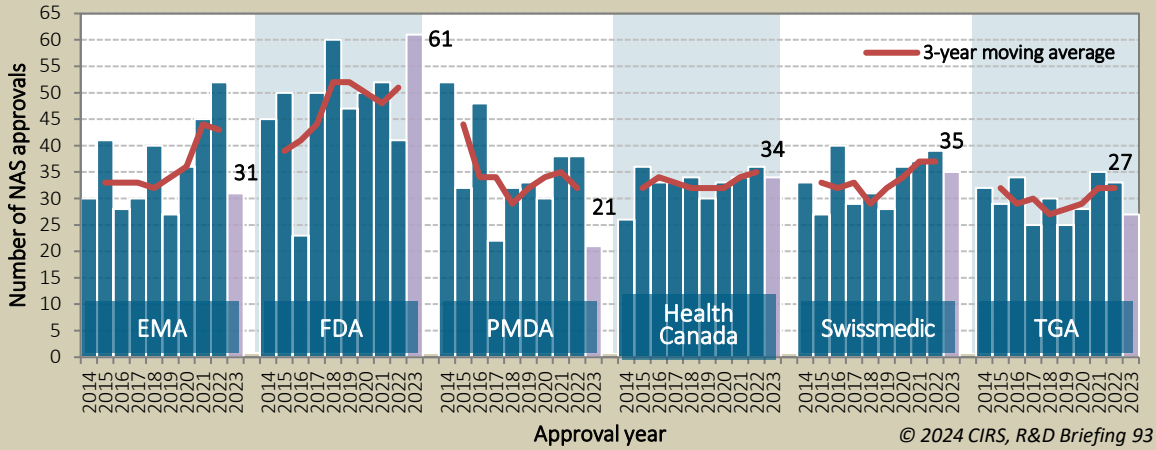
- Despite convergence in approval times over the last 20 years, there were still differences in median approval times across the six agencies (121 days between PMDA and EMA). Additionally, this difference was narrower when comparing the median time from submission to the end of the scientific assessment, as defined *on p. 20.*
- In 2023, FDA approved the highest number of NASs (61) followed by Swissmedic (35), Health Canada (34), EMA (31), TGA (27) and PMDA (21) (Fig. 1). Although FDA has consistently approved more NASs in the last ten years, not all of them get internationalised or they take a considerable amount of time to roll out to other markets (see p. 4).
- In 2023, PMDA had the shortest median approval time (332 days) with the least variance as demonstrated by an interquartile range (IQR) of 83 days. FDA followed this with 333 days (IQR of 170), Health Canada with 351 days (IQR of 183), TGA with 362 days (IQR of 95), Swissmedic with 441 days (IQR of 259) and EMA with 453 days (IQR of 119) (Fig. 2).
- In 2023, FDA had the shortest median submission gap (0 days) as companies submit there first, followed by EMA (25 days), Swissmedic (291 days), Health Canada (593 day), PMDA (644 days) and TGA (886 days) (Fig. 3).
- In 2023, the ratio of expedited approvals to standard reviews was highest for FDA (62%), followed by PMDA (33%), Health Canada (24%), Swissmedic (14%), TGA (11%) and EMA (3%) (Fig. 5). For EMA, this proportion was low, partially because the review type can be reverted to standard review by the agency if the legislated timelines cannot be met.
- EMA was the agency with the greatest difference in median approval time between expedited and standard review in 2023, with a difference of 225 days, whereas the smallest difference was for PMDA, with 76 days. The difference between standard and expedited review was 171 days for Swissmedic, 167 days for Health Canada, 121 days for FDA, and 91 days for TGA (Fig. 6).
- Anti-cancer and immunomodulators made up 42% (464/1092) of all approvals (Fig. 7). Overall, anti-infective therapies obtained the fastest median approval of the top five therapeutic areas with 295 days, followed by alimentary and metabolism therapies, which are now in second place with 322 days and anti-cancer and immunomodulator therapies in third places with 344 days. This change may be due to a shift in unmet medical needs, as reflected by the use of expedited pathways.
- Over the last five years (2019-2023), the usage of facilitated regulatory pathways (FRPs, see p.18 for definitions) has increased for most of the agencies compared with 2014-2018 (Fig. 9). FDA was the agency that used FRPs the most between 2019-2023, with 74% of NASs that had at least one FRP, followed by Swissmedic (61%), TGA (59%), Health Canada (51%), PMDA (39%) and EMA (36%).
- In 2023, the proportion of conditional/accelerated/provisional approvals was 26% for TGA, 23% for EMA, 20% for Swissmedic, 18% for Health Canada and 16% for FDA (Fig. 10). The number of conditional/ accelerated/provisional approvals has generally fluctuated year on year in 2019-2023.
- In 2023, the proportion of approved NASs with an orphan designation was high across all agencies, with 63% for Swissmedic, 56% for FDA, 44% for TGA, 35% for EMA and 29% for PMDA (Fig. 12). From 2019-2023, the proportion of orphans varied year-on-year but generally increased compared to 2014-2018.
- PMDA had the fastest median approval time for orphans in 2023 (265 days), as all these products were approved through expedited review, due to an incentive from PMDA to address unmet needs (Fig. 13). FDA had the second-fastest median approval time for orphans in 2023 (332 days), followed by Swissmedic (344 days), TGA (346 days) and EMA (441 days).
- The number of products approved by all six agencies in a five-year period decreased from 52 NASs in 2014-2018 to 38 NASs in 2019-2023, suggesting that the pace of internationalisation may be decreasing (Fig. 14). In addition, the recent increase in submission gap (seen in p.4) may also result in a further decrease in internationalisation and lead to an even lower number of NASs approved by all agencies within a similar timeframe.

See agency-specific infographics for 2023 snapshots:

EMA	FDA	PMDA	Health Canada	Swissmedic	TGA
p.12	p.13	p.14	p.15	p.16	p.17

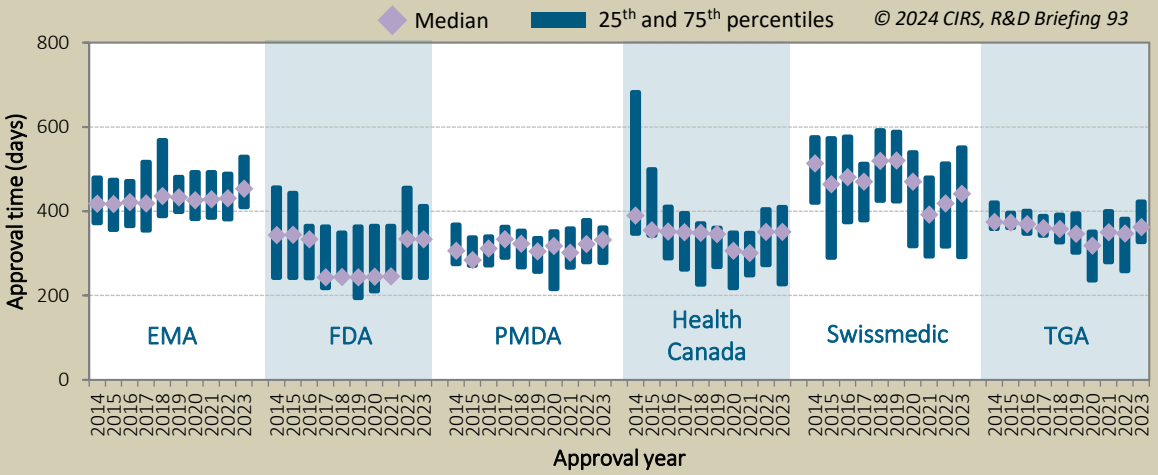
Overall approvals

Figure 1: Number of NASs approved by six regulatory authorities between 2014-2023



In 2023, FDA approved the highest number of NASs (61) followed by Swissmedic (35), Health Canada (34), EMA (31), TGA (27) and PMDA (21) (Fig. 1). Although FDA has consistently approved more NASs than the other agencies in the last ten years, not all of them get internationalised or they take a considerable amount of time to roll out to other markets (see p.4). Comparing the number of NAS approvals during the two halves of the decade, 2014-2018 and 2019-2023, revealed that the biggest change was seen for EMA, with a 13% increase, followed by FDA (10%), Swissmedic (9%), and Health Canada (3%), whereas the number of PMDA and TGA approvals decreased by 14% and 1%, respectively. The variance in the number of products approved by each agency may be explained by several factors, such as different submission strategies to each agency, depending on company size, unmet medical needs, review speed, as well as the use of risk-based pathways and collaborative/work-sharing reviews.

Figure 2: NAS approval time for six regulatory authorities between 2014-2023

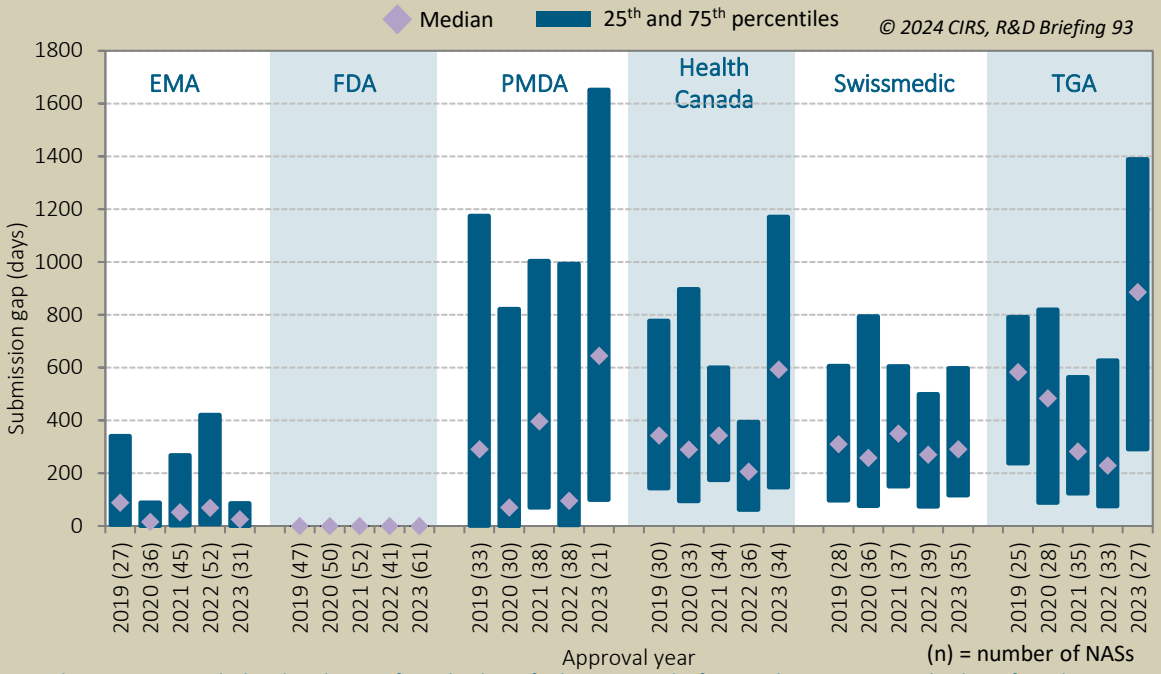


Approval time is calculated from the date of submission to the date of approval by the agency. This time includes agency and company time. EMA approval time includes the EU Commission time.

In 2023, PMDA had the shortest median approval time (332 days) as well as the shortest interquartile range (IQR) of 83 days. FDA followed this with 333 days (IQR of 170), Health Canada with 351 days (IQR of 183), TGA with 362 days (IQR of 95), Swissmedic with 441 days (IQR of 259) and EMA with 453 days (IQR of 119) (Fig.2). Despite convergence in approval times over the last 20 years (data not shown), there were still differences in median approval times across the six agencies (cover page; 121 days between PMDA and EMA). Additionally, this difference was narrower when comparing the median time from submission to the end of the scientific assessment (81 days between PMDA and EMA). The activities following the end of scientific assessment and prior to marketing authorisation are defined on pages 20 and 21. For FDA, Health Canada and TGA, the overall approval time and the time to end of the scientific assessment were the same or similar, which indicates that very few activities occur after the scientific assessment compared to EMA (see p.12) or Swissmedic. EMA's median approval time increased by 23 days compared to 2022 outcomes. The main driver of this increment was company time, where the median increased from 117 days (IQR of 70) to 127 days (IQR of 106). FDA and Health Canada's median approval times continued to be higher than outcomes reported prior to 2022, while Swissmedic kept an upward trend since 2021.

Submission gap

Figure 3: NAS submission gap for six regulatory authorities between 2019-2023



Submission gap is calculated as the time from the date of submission at the first regulatory agency to the date of regulatory submission to the target agency.

In 2023, FDA had the shortest median submission gap (0 days) as companies submit there first, followed by EMA with 25 days, Swissmedic with 291 days, Health Canada with 593 days, PMDA with 644 days and TGA with 886 days (Fig. 3). Compared with 2022, the median submission gap for EMA has decreased by 44 days, remained the same for FDA, and increased for Swissmedic by 21 days, followed by Health Canada with 388 days, PMDA by 548 days and TGA by 657 days. The submission gap was also analysed in terms of the variance around the median and IQR. For EMA, the 75th percentile for the submission gap has decreased from 420 days in 2022 to 85 days in 2023. The increase in PMDA, Health Canada, Swissmedic and TGA median submission gap was also reflected in an increase in their 25th and 75th percentiles. PMDA had the widest IQR compared to the other five agencies across 2019-2023. The shift in submission gap (median and variance) could reflect a changing trend in company strategy, or it may be due to legacy products approved in that specific year, or the size of pharmaceutical companies submitting products that year (where smaller company size often correlates with longer gap).

Figure 4: Proportion of NASs approved by a single agency between 2019-2023

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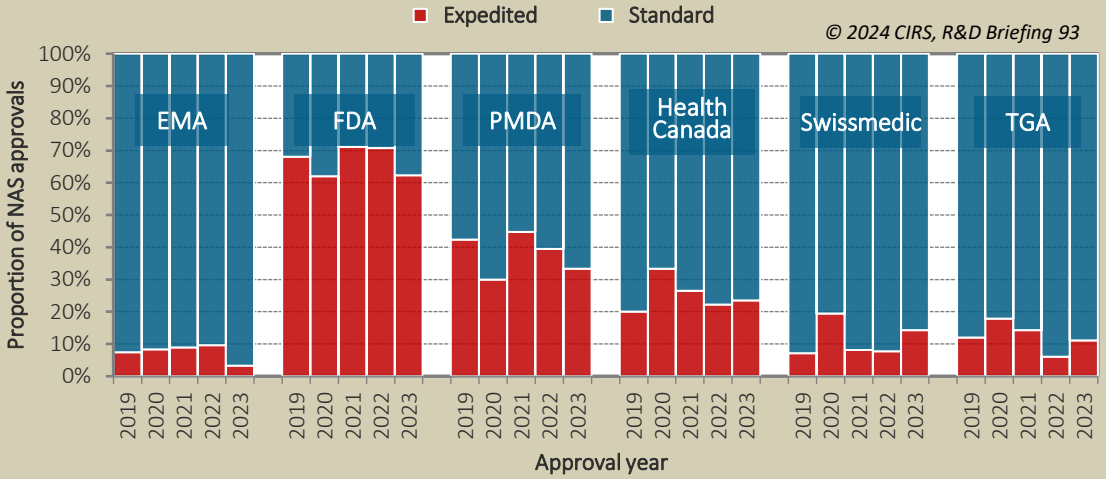
	% of NASs approved by a single agency				
Agency	**2019**	**2020**	**2021**	**2022**	**2023**
EMA	4%	6%	2%	6%	13%
FDA	15%	22%	27%	27%	57%
PMDA	15%	20%	21%	21%	0%
Health Canada	0%	0%	0%	3%	3%
Swissmedic	0%	0%	3%	0%	6%
TGA	0%	4%	0%	9%	4%

Note that this analysis is limited to products approved by the six agencies in 1997-2023; approvals outside of this year range or by other agencies (including European national approvals) were not taken into account.

The internationalisation of products was studied by comparing whether the NASs were approved by a single agency (and not by the other five agencies). In 2023, 57% of NASs approved by FDA were only approved in the US that year. Although this percentage was lower in 2019-2022, some of those products are likely to reach other agencies at a later stage. Conversely, no NAS was approved solely by PMDA in 2023.

Characteristics: Review type

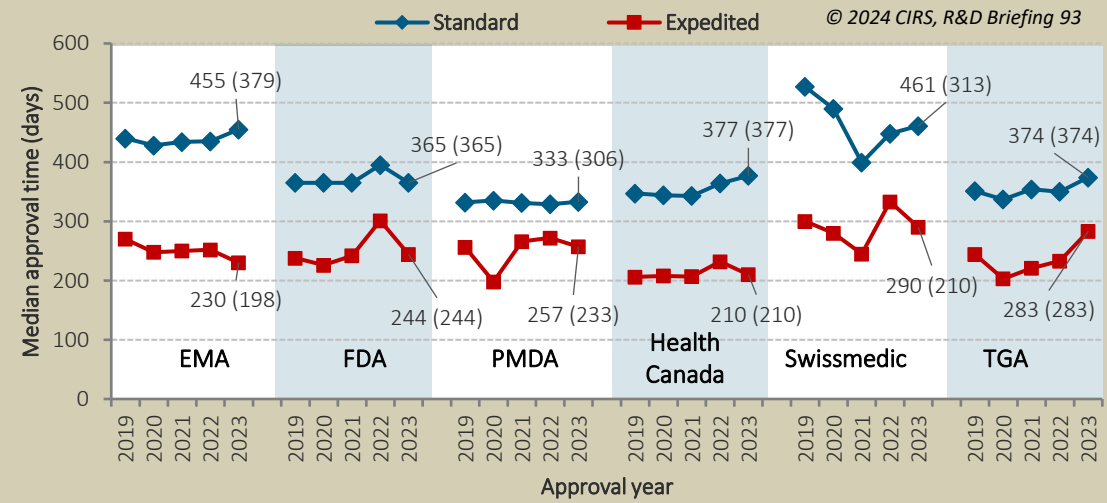
Figure 5: Number of NAS approvals by review type for six regulatory authorities between 2019-2023



'Expedited review' refers to EMA 'Accelerated Assessment', Swissmedic 'Fast Track' and FDA/PMDA/Health Canada/TGA 'Priority Review'. TGA introduced an expedited (priority) review programme in 2017.

All six agencies offer an expedited process designed to hasten the review process of promising NASs (Fig. 5). In 2023, the ratio of expedited approvals to standard reviews was highest for FDA (62%), followed by PMDA (33%), Health Canada (24%), Swissmedic (14%), TGA (11%) and EMA (3%). The proportion of expedited approvals was similar in 2023 compared to 2022 for the six agencies. In the last year, EMA approved only one NAS through an expedited approval, partially because the review type can be reverted to standard review by the agency if the legislated timelines cannot be met. For instance, in 2023, two NASs initially designated by EMA as expedited were reverted, whereas, for three NASs, the applicant requested expedited review, but these NASs were not deemed eligible by EMA.

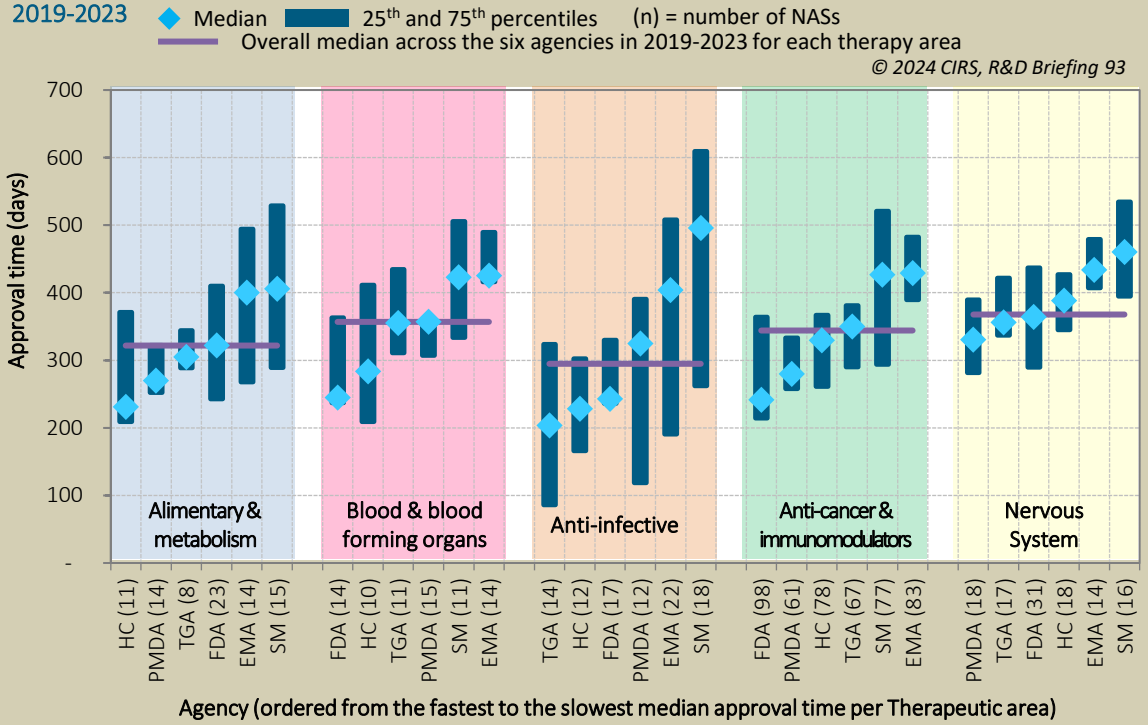
Figure 6: NAS median approval time by review type for six regulatory authorities between 2019-2023



'Expedited review' refers to EMA 'Accelerated Assessment', Swissmedic 'Fast Track' and FDA/PMDA/Health Canada/TGA 'Priority Review'. TGA introduced an expedited (priority) review programme in 2017. Approval time is calculated from the date of submission to the date of approval by the agency. This time includes agency and company time. EMA approval time includes the EU Commission time. N1 = overall approval time for 2023; (N2) = time from submission until the end of scientific assessment (see p.20) for 2023.

EMA was the agency with the greatest difference in median approval time between expedited and standard review in 2023, with a difference of 225 days, whereas the smallest difference was for PMDA, with 76 days. The difference between standard and expedited review was 171 days for Swissmedic, 167 days for Health Canada, 121 days for FDA, and 91 days for TGA (Fig.6). In 2023, the EMA's median time until the end of scientific assessment for NAS approved through an expedited review was 198 days, 181 days lower than those approved through a standard review. The median authorisation process (European Commission) time for expedited-approved NASs took 32 days, compared to 76 days for standard. Although the Swissmedic median time from submission until the end of scientific assessment was 210 days for expedited in 2023, an additional 80 days were needed to receive marketing authorisation due to a labelling process. Both EMA and Swissmedic have been implementing measures to accelerate the authorisation processes further.

Figure 7: NAS median approval time by top five therapeutic areas (TAs) for six regulatory authorities between 2019-2023



Therapy areas relate to the WHO ATC codes. Approval time is calculated from the date of submission to the date of approval bythe agency. This time includes agency and company time. EMA approval time includes the EU Commission time.

The top five TAs by number of NASs approved across all six agencies made up 76% (833/1092) of all approvals between 2019-2023, with anti-cancer and immunomodulators making up 42% (464/1092) of all approvals (Fig. 7). Anti-infective therapies obtained the fastest median global approval of the top five therapeutic areas with 295 days. When comparing the overall median approval times reported in previous briefings (R&D 81, 85 and 88), it appears that the gap between the overall median approval time of anti-infective therapies versus other therapeutic areas has widened, which may be due to products approved for COVID. On the other hand, alimentary and metabolism therapies are now in second place together with anti-cancer and immunomodulator therapies, with an overall median approval time of 322 and 344 days, respectively, which may be due to a shift in unmet medical needs. In fact, the % of alimentary and metabolism NASs reviewed as expedited increased from 23% in 2014-2018 to 41% in 2019-2023.

Figure 8: NAS overall median approval time by top five therapeutic areas in relation to expedited approvals for six regulatory authorities between 2019-2023

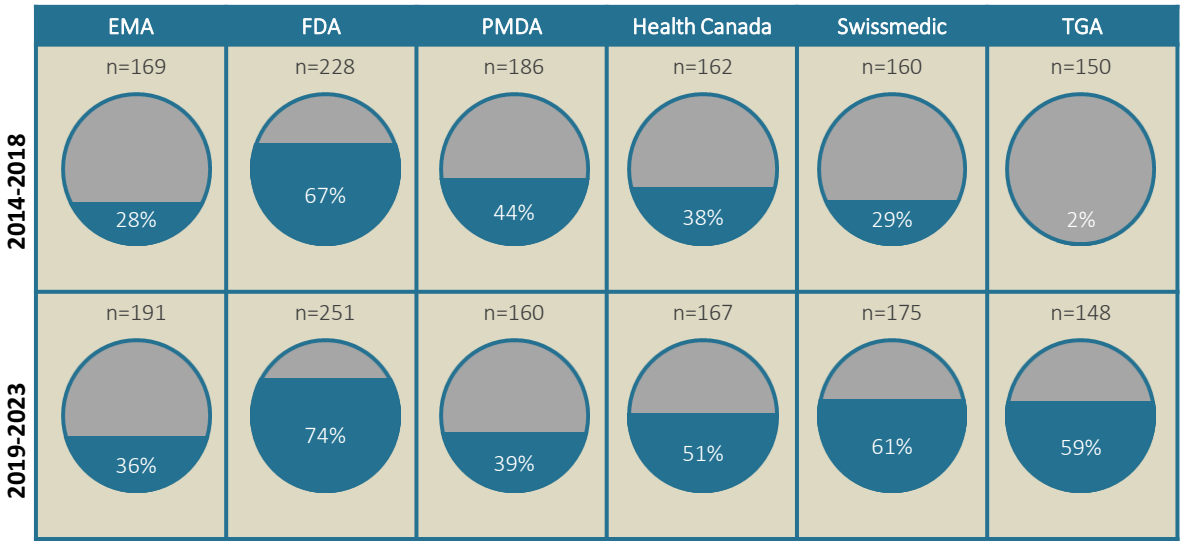
© 2024 CIRS, R&D Briefing 93	Alimentary and metabolism	Blood and blood forming organs	Anti-infective	Anti-cancer and immuno-modulators	Nervous system
	Approval time in days (proportion of expedited approvals)				
EMA	400 (29%)	426 (7%)	404 (5%)	429 (10%)	434 (0%)
FDA	322 (65%)	245 (79%)	243 (94%)	242 (76%)	364 (39%)
PMDA	270 (64%)	357 (40%)	325 (58%)	280 (49%)	331 (17%)
Health Canada	231 (55%)	284 (50%)	228 (33%)	330 (19%)	389 (17%)
Swissmedic	406 (7%)	423 (18%)	496 (0%)	427 (13%)	461 (13%)
TGA	305 (0%)	355 (18%)	204 (14%)	350 (12%)	356 (6%)

Therapeutic areas relate to the WHO ATC codes. 'Expedited review' refers to EMA 'Accelerated Assessment', Swissmedic 'Fast Track' and FDA/PMDA/Health Canada/TGA 'Priority Review'. Approval time is calculated from the date of submission to the date of approval by the agency. This time includes agency and company time. EMA approval time includes the EU Commission time.

Focus on facilitated regulatory pathways (FRPs)

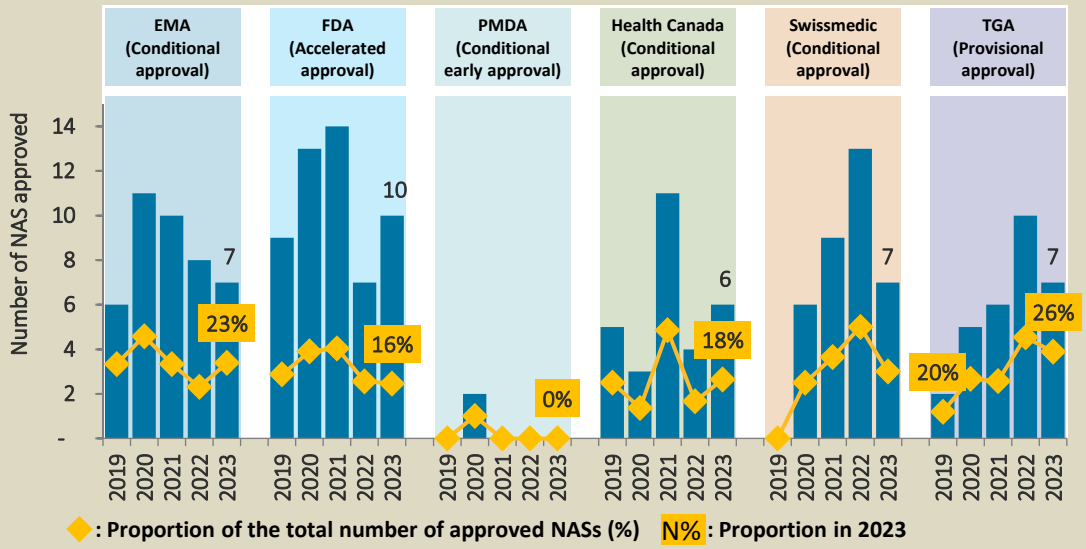
Over the last five years (2019-2023), the usage of facilitated regulatory pathways (FRPs, see p.18 for definitions) has increased for most of the agencies compared with the beginning of the decade (2014-2018) (Fig. 9). FDA was the agency that used FRPs the most between 2019-2023, with 74% of NASs approved with at least one FRP, followed by Swissmedic (61%), TGA (59%), Health Canada (51%), PMDA (39%) and EMA (36%). TGA was the agency that has seen the biggest increase in terms of the percentage of NAS approvals with FRPs, which demonstrates the recent implementation of the five FRPs by TGA (starting in 2017 with Priority review, Provisional approvals, Comparable overseas regulators (COR) review, Access Work-sharing Consortium, and Project Orbis). PMDA was the only agency where the proportion of NASs approved with an FRP decreased (by five percentage points) when comparing 2014-2018 and 2019-2023.

Figure 9: Proportion of NAS approved by each agency between 2014-2018 vs 2019-2023 that benefited from an FRP



In 2023, the proportion of conditional/accelerated/provisional approvals was 26% for TGA, 23% for EMA, 20% for Swissmedic, 18% for Health Canada and 16% for FDA (Fig. 10). The number of conditional/ accelerated/provisional approvals has generally fluctuated year on year in 2019-2023. In general, these types of approval pathways were faster than the overall median approval time for all six regulatory agencies (Fig. 11, on p8) which may be due to the use of expedited pathways.

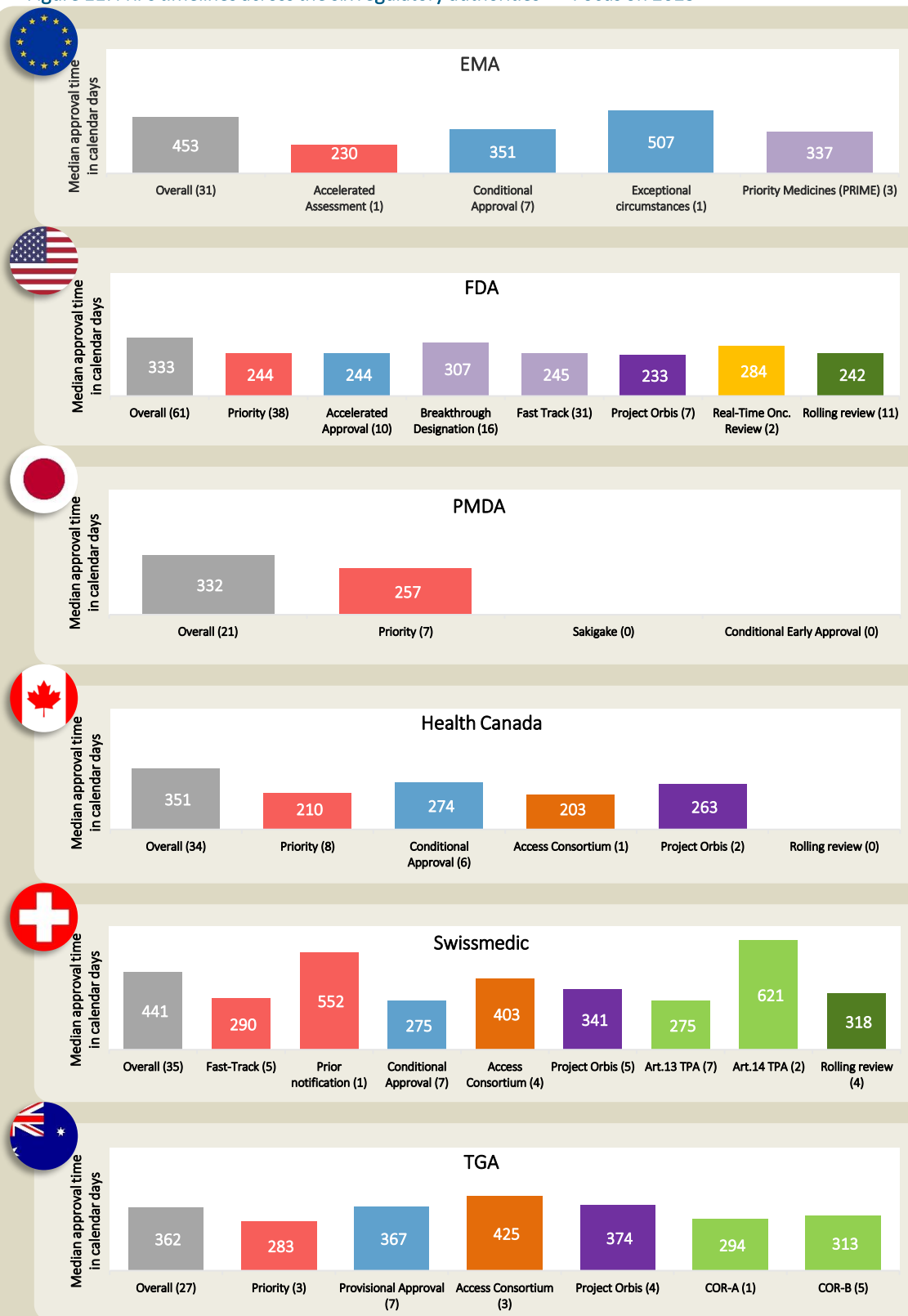
Figure 10: Number of NAS approved through a conditional/accelerated/provisional approval pathway by the six regulatory authorities between 2019-2023



The 2023 NAS median approval times for the different FRPs are illustrated on the next page (Fig. 11).

Focus on facilitated regulatory pathways (FRPs) *(cont.)*

Figure 11: FRPs timelines across the six regulatory authorities — Focus on 2023



(n) = number of NASs

Expedited Review

Conditional/accelerated/ provisional approvals

Earlier/ Intensive dialogue review

Real time review

Collaborative Review

Reliance/ Abridged/ Simplified review

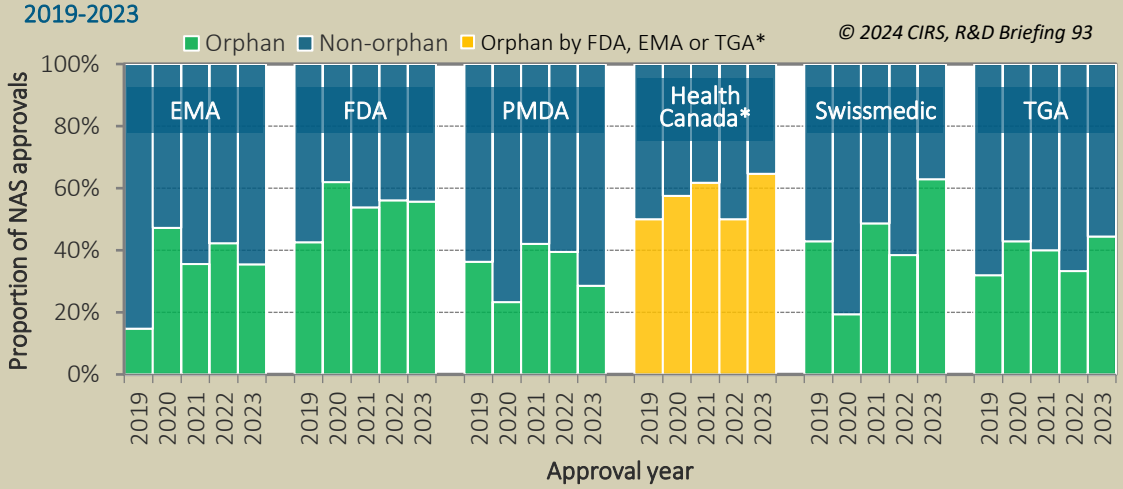
Work-sharing Review

Rolling review

For FRP definitions see p.18.

Focus on orphan designations

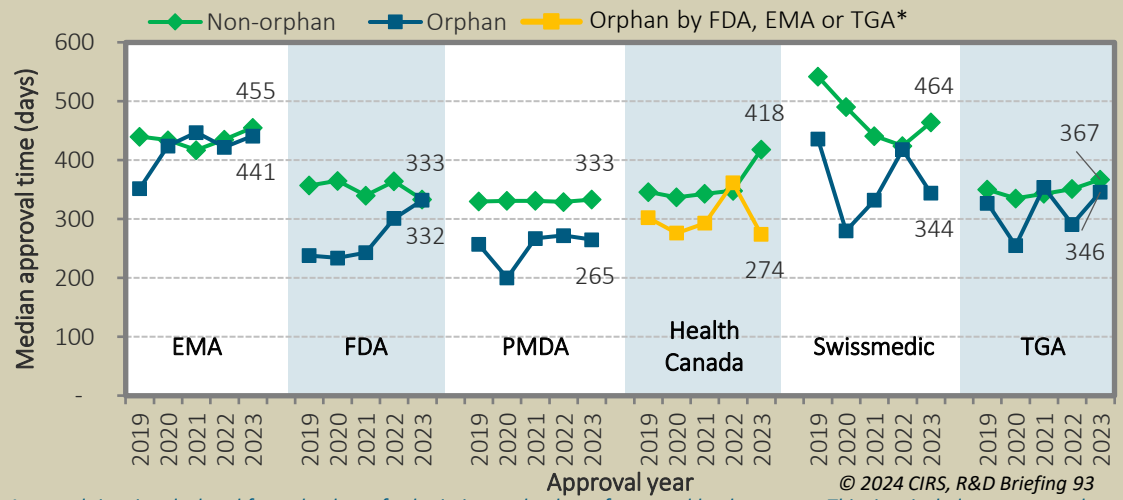
Figure 12: Proportion of NAS approvals by orphan designation for six regulatory authorities between 2019-2023



** Health Canada does not currently have an orphan policy; this data shows the number of medicines that were approved by Health Canada that were classified as orphan by either FDA, EMA or TGA.*

In 2023, the proportion of approved NASs with an orphan designation was high across all agencies, with 63% for Swissmedic, 56% for FDA, 44% for TGA, 35% for EMA and 29% for PMDA (Fig. 12).
From 2019-2023, the proportion of orphans varied year-on-year but generally increased compared to 2014-2018 where the proportion of NASs approved with an orphan designation was 32% for Swissmedic, 49% for FDA, 29% for TGA, 39% for EMA and 34% for PMDA. This may be due to disease stratification and companies' growing R&D pipelines; it is also consistent with increased commitment from agencies to tackle unmet medical needs. The variance across agencies may be due to a variety of factors, such as differences in orphan designation criteria across the agencies or the indication submitted by the sponsor.

Figure 13: NAS median approval time by review type for six regulatory authorities between 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. EMA approval time includes the EU Commission time.
**Health Canada does not currently have an orphan policy; this data shows the number of medicines that were approved by Health Canada that were classified as orphan by either FDA, EMA or TGA.*

Approval timelines for orphans and non-orphans were compared across the six agencies between 2019-2023 (Fig. 13). PMDA had the fastest median approval time for orphans in 2023 (265 days), as all these products were approved through expedited review, due to an incentive from PMDA to address unmet needs. FDA had the second-fastest median approval time for orphans in 2023 (332 days), followed by Swissmedic (344 days), TGA (346 days), and EMA (441 days). For EMA and TGA, the median times for orphans compared to non-orphans have been similar for most years between 2019-2023, and this may be due to similar use of expedited pathways regardless of orphan designation. Health Canada does not currently have an orphan policy; however, for the 22 NASs approved by Health Canada in 2023 that were classified as orphan by either FDA, EMA or TGA, the median approval time was 274 days.

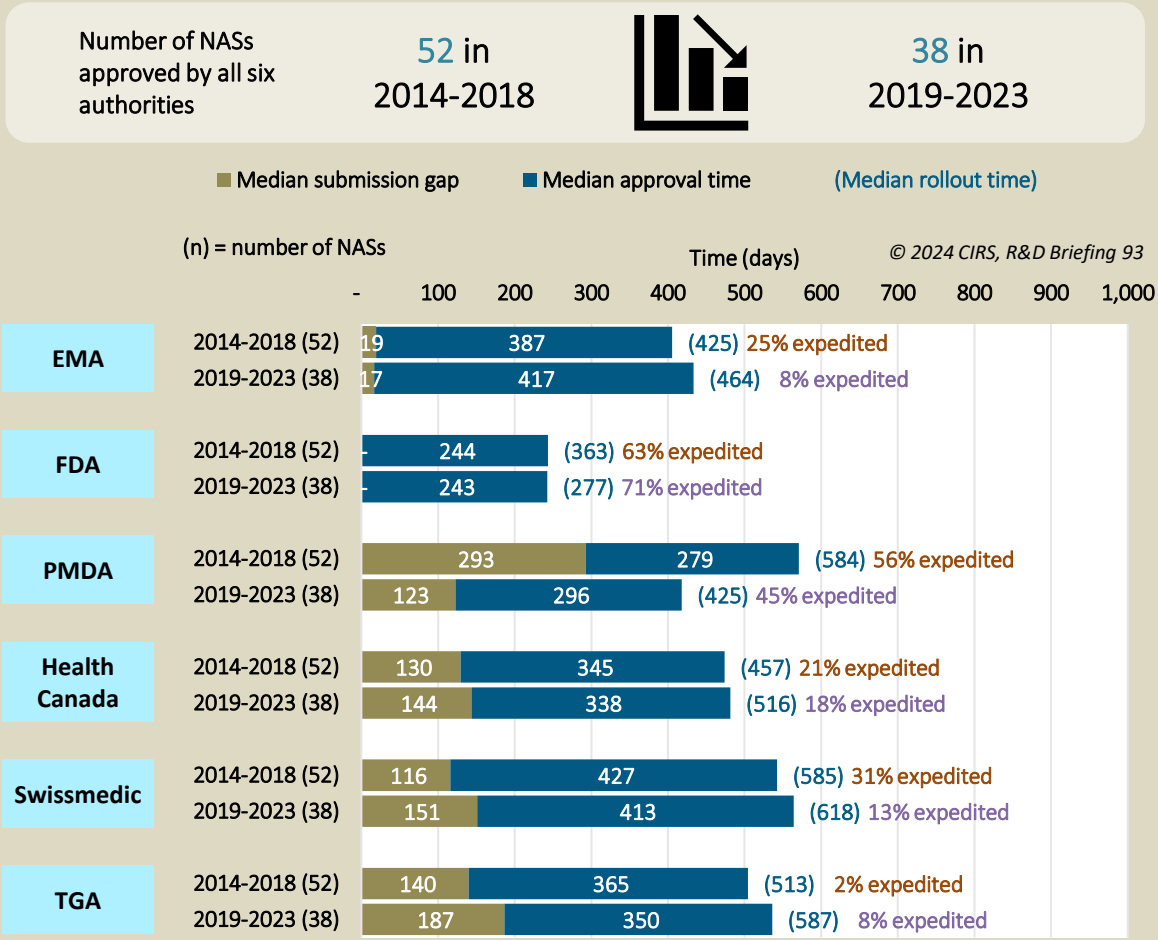
Common approvals across the six regulatory agencies

In order to have a true regulatory performance benchmark assessment, it is important to review the compounds that were approved by all six agencies. This assessment was carried out for both time cohorts in the last decade (2014-2018 and 2019-2023) to identify trends. The number of products approved by all six agencies in a five-year period decreased from 52 NASs in 2014-2018 to 38 NASs in 2019-2023, which was also seen in recent years' analyses (see R&D Briefing 88 and 85). This contrasts with analyses in previous years where there was an increase (see R&D Briefing 70 and 77), suggesting that the pace of internationalisation may be decreasing. In addition, the recent increase in submission gap (seen in p.4) may also result in a further decrease in internationalisation and lead to an even lower number of NASs approved by all agencies within a similar timeframe.

The rollout time, consisting of the submission gap and approval time (Fig. 14), can be influenced by a number of factors such as company submission strategy and the use of expedited pathways to address unmet medical needs. The fastest overall median rollout time for the 2019-2023 cohort was for FDA with 277 days, as a result of companies submitting there first and quick regulatory review times due to the wider use of expedited reviews (71% of approved NASs). This was followed by PMDA with 425 days, EMA with 464 days, Health Canada with 516 days, TGA with 587 days, and Swissmedic with 618 days.

Submission to EMA occurred almost simultaneously with FDA, followed by PMDA, Health Canada, Swissmedic and TGA. Compared to past R&D Briefings, this Briefing suggests that there has been a change in the waves of submission to agencies, where submission to PMDA was previously found to be later than the submission to Health Canada, Swissmedic, and TGA, but it is now more in line with those agencies. Indeed, the median submission gap to PMDA has reduced from 293 days in 2014-2018 to 123 days in 2019-2023.

Figure 14: Median submission gap and median approval time for NASs approved by all six authorities in 2014-2018 (52) compared with 2019-2023 (38), as well as their expedited review proportion



Submission gap is calculated as the time from the date of submission at the first regulatory agency 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. EMA approval time includes the EU Commission 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. 'Expedited review' refers to EMA 'Accelerated Assessment', Swissmedic 'Fast Track' and FDA/PMDA/Health Canada/TGA 'Priority Review'.

Summary of NAS approved in 2023 by the six agencies

This table summarises approval times for NASs approved in 2023 by the six agencies, broken down by product type, review type and major therapeutic area.

Agency Median approval time in calendar days	EMA  p.12	FDA  p.13	PMDA  p.14	Health Canada  p.15	Swissmedic  p.16	TGA  p.17
Number of NAS approved	31	61	21	34	35	27
NAS overall approval time (days)	453	333	332	351	441	362
By biologics (days)	430	320	304	274	341	362
By chemicals (days)	457	334	333	400	465	374
By standard review (days)	455	365	333	377	461	374
By expedited review (days)	230	244	257	210	290	283
By orphans (days)	441	332	265	274*	344	346
By anticancer and immuno-modulators (days)	431	244	319	346	354	374

Approval time is calculated from the date of submission to the date of approval by the agency. This time includes agency and company time. EMA approval time includes the EU Commission time.
** Health Canada does not have an orphan policy; however, in 2023, Health Canada approved 22 NASs classified as orphan by either the FDA, EMA, or TGA, with a median approval time of 274 days.*

EMA **APPROVED A TOTAL OF 31 NASs IN 2023,** WITH A MEDIAN APPROVAL TIME OF **453 DAYS AND A MEDIAN TIME TO END OF SCIENTIFIC ASSESSMENT OF 378 DAYS**

THE MEDIAN EU COMMISSION TIME WAS 61 DAYS, THE EMA REVIEW TIME 240 DAYS AND THE COMPANY TIME 127 DAYS

Type of Medicine

12 BIOLOGIC NASs APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **430 DAYS**

19 CHEMICAL NASs APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **457 DAYS**

17 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **431 DAYS**

14 NASs IN OTHER THERAPY AREAS APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **489 DAYS**

Designation and Review Type

1 EXPEDITED NAS APPROVAL IN 2023, WITH AN APPROVAL TIME OF **230 DAYS;** THIS IS **225 DAYS FASTER** THAN THE MEDIAN OF THE **30 STANDARD NAS APPROVALS IN 2023**

11 ORPHAN NAS APPROVALS IN 2023, WITH A MEDIAN APPROVAL TIME OF **441 DAYS;** THIS IS **14 DAYS FASTER** THAN THE MEDIAN OF THE 20 **NON-ORPHAN NAS APPROVALS IN 2023**

Availability by EMA

16% OF THE NASs APPROVED IN 2023 BY EMA WERE APPROVED FIRST BY THE AGENCY OR WITHIN ONE MONTH OF FIRST APPROVAL BY ANY OF THE OTHER AGENCIES

84% OF THE NASs APPROVED IN 2023 BY EMA WERE APPROVED BY ANY OF THE OTHER AGENCIES **FIRST OR MORE THAN ONE MONTH BEFORE BEING APPROVED BY THE AGENCY**

THE MEDIAN **SUBMISSION GAP** TO EMA FOR THESE NASs WAS **30 DAYS**

Approval time is calculated from the date of submission to the date of approval by the agency. This time includes agency and company time. EMA approval time includes the EU Commission time. 'Expedited review' refers to EMA 'Accelerated Assessment. Submission gap is the date of submission at the first regulatory agency to the date of regulatory submission to the target agency.

FDA (CDER AND CBER) **APPROVED A TOTAL OF 61 NASs IN 2023,** WITH A MEDIAN APPROVAL TIME OF **333 DAYS**

82% OF THE NAS APPROVALS WERE GRANTED BY THE FDA IN THE FIRST SCIENTIFIC REVIEW CYCLE

Type of Medicine

27 BIOLOGIC NASs APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **320 DAYS**

34 CHEMICAL NASs APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **334 DAYS**

21 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **244 DAYS**

40 NASs IN OTHER THERAPY AREAS APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **335 DAYS**

Designation and Review Type

38 EXPEDITED NAS APPROVALS IN 2023, WITH A MEDIAN APPROVAL TIME OF **244 DAYS;** THIS IS **121 DAYS FASTER** THAN THE MEDIAN OF THE **23 STANDARD NAS APPROVALS IN 2023**

34 ORPHAN NAS APPROVALS IN 2023, WITH A MEDIAN APPROVAL TIME OF **332 DAYS;** THIS IS **2 DAYS FASTER** THAN THE MEDIAN OF THE **27 NON-ORPHAN NAS APPROVALS IN 2023**

Availability by FDA

80% OF THE NASs APPROVED IN 2023 BY FDA WERE APPROVED FIRST BY THE AGENCY OR WITHIN ONE MONTH OF FIRST APPROVAL BY ANY OF THE OTHER AGENCIES

20% OF THE NASs APPROVED IN 2023 BY FDA WERE APPROVED BY ANY OF THE OTHER AGENCIES **FIRST OR MORE THAN ONE MONTH BEFORE BEING APPROVED BY THE AGENCY**

THE MEDIAN **SUBMISSION GAP** FOR THESE NASs WAS **220 DAYS**

'Expedited review' refers to FDA 'Priority Review'. Submission gap is the date of submission at the first regulatory agency to the date of regulatory submission to the target agency.

PMDA **APPROVED A TOTAL OF 21 NASs IN 2023,** WITH A MEDIAN APPROVAL TIME OF **332 DAYS AND A MEDIAN TIME TO END OF SCIENTIFIC ASSESSMENT OF 297 DAYS**

Type of Medicine

9 BIOLOGIC NASs APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **304 DAYS**

12 CHEMICAL NASs APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **333 DAYS**

8 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **319 DAYS**

13 NASs IN OTHER THERAPY AREAS APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **332 DAYS**

Designation and Review Type

7 EXPEDITED NAS APPROVALS IN 2023, WITH A MEDIAN APPROVAL TIME OF **257 DAYS;** THIS IS **76 DAYS FASTER** THAN THE MEDIAN OF THE **14 STANDARD NAS APPROVALS IN 2023**

6 ORPHAN NAS APPROVALS IN 2023, WITH A MEDIAN APPROVAL TIME OF **265** THIS IS **68 DAYS FASTER** THAN THE MEDIAN OF THE **15 NON-ORPHAN NAS APPROVALS IN 2023**

Availability by PMDA

14% OF THE NASs APPROVED IN 2023 BY PMDA WERE APPROVED FIRST BY THE AGENCY OR WITHIN ONE MONTH OF FIRST APPROVAL BY ANY OF THE OTHER AGENCIES

86% OF THE NASs APPROVED IN 2023 BY PMDA WERE APPROVED BY ANY OF THE OTHER AGENCIES **FIRST OR MORE THAN ONE MONTH BEFORE BEING APPROVED BY THE AGENCY**

THE MEDIAN **SUBMISSION GAP** FOR THESE NASs WAS **882 DAYS**

'Expedited review' refers to PMDA 'Priority Review'. Submission gap is the date of submission at the first regulatory agency to the date of regulatory submission to the target agency.

HEALTH CANADA **APPROVED A TOTAL OF 34 NASs IN 2023,** WITH A MEDIAN APPROVAL TIME OF **351 DAYS AND A MEDIAN TIME TO END OF SCIENTIFIC ASSESSMENT OF 351 DAYS**

Type of Medicine

19 BIOLOGIC NASs APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **274 DAYS**

15 CHEMICAL NASs APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **400 DAYS**

12 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **346 DAYS**

22 NASs IN OTHER THERAPY AREAS APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **352 DAYS**

Designation and Review Type

8 EXPEDITED NAS APPROVALS IN 2023, WITH A MEDIAN APPROVAL TIME OF **210 DAYS;** THIS IS **168 DAYS FASTER** THAN THE MEDIAN OF THE **26 STANDARD NAS APPROVALS IN 2023**

HEALTH CANADA DOES NOT HAVE AN ORPHAN POLICY; HOWEVER, **22 NASs THAT WERE CLASSIFIED AS ORPHAN BY EITHER FDA, EMA OR TGA WERE APPROVED BY HEALTH CANADA IN 2023,** WITH A MEDIAN APPROVAL TIME OF **274 DAYS**

Availability by Health Canada

9% OF THE NASs APPROVED IN 2023 BY HEALTH CANADA WERE APPROVED FIRST BY THE AGENCY OR WITHIN ONE MONTH OF FIRST APPROVAL BY ANY OF THE OTHER AGENCIES

91% OF THE NASs APPROVED IN 2023 BY HEALTH CANADA WERE APPROVED BY ANY OF THE OTHER AGENCIES **FIRST OR MORE THAN ONE MONTH BEFORE BEING APPROVED BY THE AGENCY**

THE MEDIAN **SUBMISSION GAP** FOR THESE NASs WAS **698 DAYS**

'Expedited review' refers to Health Canada's 'Priority Review'. Submission gap is the date of submission at the first regulatory agency to the date of regulatory submission to the target agency.

SWISSMEDIC **APPROVED A TOTAL OF 35 NASs IN 2023,** WITH A MEDIAN APPROVAL TIME OF **441 DAYS AND A MEDIAN TIME TO END OF SCIENTIFIC ASSESSMENT OF 308 DAYS**

Type of Medicine

17 BIOLOGIC NASs APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **341 DAYS**

18 CHEMICAL NASs APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **465 DAYS**

15 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **354 DAYS**

20 NASs IN OTHER THERAPY AREAS APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **458 DAYS**

Designation and Review Type

5 EXPEDITED NAS APPROVALS IN 2023, WITH A MEDIAN APPROVAL TIME OF **290 DAYS;** THIS IS **171 DAYS FASTER** THAN THE MEDIAN OF THE **30 STANDARD NAS APPROVALS IN 2023**

22 ORPHAN NAS APPROVALS IN 2023, WITH A MEDIAN APPROVAL TIME OF **344 DAYS;** THIS IS **120 DAYS FASTER** THAN THE MEDIAN OF THE **13 NON-ORPHAN NAS APPROVALS IN 2023**

Availability by Swissmedic

11% OF THE NASs APPROVED IN 2023 BY SWISSMEDIC WERE APPROVED FIRST BY THE AGENCY OR WITHIN ONE MONTH OF FIRST APPROVAL BY ANY OF THE OTHER AGENCIES

89% OF THE NASs APPROVED IN 2023 BY SWISSMEDIC WERE APPROVED BY ANY OF THE OTHER AGENCIES **FIRST OR MORE THAN ONE MONTH BEFORE BEING APPROVED BY THE AGENCY**

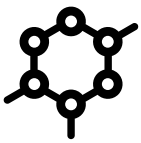
THE MEDIAN **SUBMISSION GAP** FOR THESE NASs WAS **351 DAYS**

'Expedited review' refers to the 'Fast-Track procedure' of Swissmedic. Submission gap is the date of submission at the first regulatory agency to the date of regulatory submission to the target agency.

TGA **APPROVED A TOTAL OF 27 NASs IN 2023,** WITH A MEDIAN APPROVAL TIME OF **362 DAYS AND A MEDIAN TIME TO END OF SCIENTIFIC ASSESSMENT OF 362 DAYS**

Type of Medicine

13 BIOLOGIC NASs APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **362 DAYS**

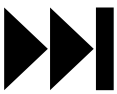


14 CHEMICAL NASs APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **374 DAYS**

12 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **374 DAYS**

15 NASs IN OTHER THERAPY AREAS APPROVED IN 2023, WITH A MEDIAN APPROVAL TIME OF **362 DAYS**

Designation and Review Type



3 EXPEDITED NAS APPROVALS IN 2023, WITH A MEDIAN APPROVAL TIME OF **283 DAYS;** THIS IS **91 DAYS FASTER** THAN THE MEDIAN OF THE **24 STANDARD NAS APPROVALS IN 2023**

12 ORPHAN NAS APPROVALS IN 2023, WITH A MEDIAN APPROVAL TIME OF **346 DAYS;** THIS IS **22 DAYS FASTER** THAN THE MEDIAN OF THE **15 NON-ORPHAN NAS APPROVALS IN 2023**

Availability by TGA

4% OF THE NASs APPROVED IN 2023 BY TGA WERE APPROVED FIRST BY THE AGENCY OR WITHIN ONE MONTH OF FIRST APPROVAL BY ANY OF THE OTHER AGENCIES

96% OF THE NASs APPROVED IN 2023 BY TGA WERE APPROVED BY ANY OF THE OTHER AGENCIES **FIRST OR MORE THAN ONE MONTH BEFORE BEING APPROVED BY THE AGENCY**

THE MEDIAN **SUBMISSION GAP** FOR THESE NASs WAS **924 DAYS**

'Expedited review' refers to the 'Priority Review' of TGA introduced in 2017. Submission gap is the date of submission at the first regulatory agency to the date of regulatory submission to the target agency.

Definitions: Facilitated regulatory pathways

	What is it?	Advantage
FDA Priority Review	A process that directs resources to the evaluation of drugs that represent significant improvements in safety or effectiveness compared with standard applications	• Review time shortened from 10 to 6 months
FDA Accelerated Approval	Regulation allowing drugs for serious conditions that fulfil an unmet medical need to be approved based on a surrogate endpoint	• Conditional approval granted using surrogate endpoint(s) from phase 2 trials or interim phase 3 data; confirmatory trials with hard clinical endpoints required
FDA Fast Track	A process designed to facilitate the development and expedite the review of drugs to treat serious conditions and fulfil an unmet medical need	• More frequent meetings with FDA to discuss drug development plan • More frequent communication on clinical trials design • Option for rolling data submission
FDA Breakthrough Therapy	A process designed to expedite the development and review of drugs that may demonstrate substantial improvement over available therapy	• All Fast Track designation features • Intensive guidance on an efficient drug development program from phase 1 • Organisational commitment with senior managers • Option for priority review
Real-Time Oncology Review (RTOR)	A programme launched by the FDA Oncology Center of Excellence (OCE), it allows FDA to access and review key data ahead of time, prior to official submission	• RTOR allows the FDA to review much of the data earlier, before the applicant formally submits the complete application.
EMA Accelerated Assessment	A process designed to expedite products of major interest in terms of public health and therapeutic innovation	• Committee for Medicinal Products for Human Use (CHMP) opinion shortened from 210 days to 150 days
EMA Conditional Approval	Regulation allowing drugs fulfilling unmet medical need for severe, life-threatening or rare diseases to be approved with limited clinical safety or efficacy data, provided a positive benefit-risk balance	• Conditional approval is granted before all data are available (valid for one year, on a renewable basis; once pending studies are provided, it can become a “normal” marketing authorisation)
EMA Exceptional Circum-stances	Regulation allowing drugs fulfilling unmet medical need for severe, life-threatening or rare diseases to be approved without comprehensive efficacy and safety data	• Conditional approval is granted before all data are available (reviewed annually to re-assess the risk-benefit balance)
EMA PRIME (Priority Medicines)	A scheme to enhance support for the development of medicines that target an unmet medical need. It is based on enhanced interaction and early dialogue with developers of promising medicines, to optimise development and speed evaluation.	• Early dialogue with EMA (appointed rapporteur) • Provision of scientific advice, involving additional stakeholders (e.g. HTA) • Dedicated point of contact from EMA • Option of Accelerated Assessment
PMDA Priority Review	A process that provides faster access to new therapies responding to high medical needs; includes products such as orphans, HIV medicines	• Review time shortened from 9 to 6 months
PMDA Conditional Early Approval	A system to put highly useful and effective drugs for treating serious diseases into practical use as early as possible	• Early application through confirmation of a certain degree of efficacy and safety • Shorten overall review times for priority review products
PMDA Sakigake (pioneer)	A system to put highly useful and effective drugs for treating serious diseases into practical use as early as possible	• All Priority Review designation features • Prioritised clinical trial and pre-application consultation • Assigned PMDA manager as a concierge • Post-marketing safety measures

Definitions: Facilitated regulatory pathways *(cont.)*

	What is it?	Advantage
Health Canada Priority	A fast-track status for medicines for severe, debilitating or life-threatening disease; to address unmet medical need and where a high therapeutic benefit can be expected	• Review time shortened from 300 to 180 days
Health Canada Conditional (NOC/c)	Authorisation to market a new promising drug with the condition that the sponsor undertakes additional studies to verify the clinical benefit	• Earlier marketing of promising drugs for serious conditions before the drugs have definitively demonstrated clinical efficacy
Swissmedic Fast-Track	A rapid review of applications for severe, debilitating or life-threatening disease; to address unmet medical need and where a high therapeutic benefit can be expected	• Review time shortened from 330 to 140 days
Temporary authorisation (Art. 9a TPA)	Temporary and conditioned authorisation of medicinal products for life-threatening or debilitating diseases, if they are compatible with health protection, a major therapeutic benefit can be expected, and no therapeutic alternative is available in Switzerland.	• Review time shortened from 330 to 140 days • A temporary authorisation granted for a maximum of two years
Swissmedic Prior Notification	A process to enable applicants to notify their submission date at an early stage, so that Swissmedic can draw up a streamlined and precise schedule for the review	• 20% faster processing time and fixed planning offered by this procedure are subject to a fee surcharge of 100%
Art.13 TPA	A process to authorise medicinal products that have already been approved in a country with a comparable medicinal product control system, taking account of the results of the trials conducted for this purpose provided that some requirements are satisfied	• In justified cases Swissmedic may reduce the scale of scientific assessments, either on request or ex officio, based on the result of the corresponding assessment by the foreign authority (e.g. USA FDA or EMA)
Art.14 TPA	An authorisation procedure for medicinal products with active substances that has been authorised in an EU or EFTA country for at least 10 years	• A simplified procedure where a review of original clinical documentation is generally only admissible for bioequivalence studies, e.g. where the pharmaceutical forms differ
TGA Priority	A formal mechanism for faster assessment of vital and life-saving medicines for severe, debilitating or life-threatening disease, to address unmet medical need and where a high therapeutic benefit can be expected	• Review time shortened from 220 to 150 working days • Dynamic process with rolling questions and more flexible arrangements for accessing advice
TGA Provisional Approval	Time-limited provisional registration for certain promising new medicines where the benefit of early availability of the medicine outweighs the risk inherent in the fact that additional data are still required	• Conditional approval is granted based on preliminary clinical data (valid for a maximum of 6 years)
Comparable overseas regulators (CORs)	The TGA makes use of assessments from comparable overseas regulators (CORs), where possible, in the regulation of prescription medicines.	Shortened evaluation and decision timeframe for prescription medicines that have already been approved by a COR partner: • For COR-A the timeframe is 120 working days • For COR-B the timeframe is 175 working days
Access Consortium	Medium-sized coalition to promote greater regulatory collaboration and alignment of regulatory requirements between Australia-Canada-Singapore-Switzerland-UK	• Maximises international cooperation, reduce duplication, and increase each agency's capacity to ensure consumers have timely access to high quality, safe and effective therapeutic products. • Maximises the use of up-to-date technical expertise, and ensures a consistent, contemporary approach to assessing the benefits and risks associated with the use of therapeutic products
Project Orbis	An initiative of the FDA Oncology Center of Excellence (OCE), provides a framework for concurrent submission and review of oncology products among international partners –Australia-Brazil-Canada-Singapore-Switzerland-UK-US	

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

Biological/Biotechnology product
A substance isolated from animal tissues or product produced by recombinant DNA or hybridoma technology and expressed in cell lines, transgenic animals or transgenic plants for therapeutic, prophylactic or in vivo diagnostic use in humans.

Chemical entity
An entity produced by chemical synthesis.

Company response time
Time calculated as the sum of periods between the date the CHMP agrees on the consolidated List of Questions/ List of Outstanding Issues to be sent to the applicant and the date in which the applicant submits the responses.

Development time
Time calculated from the date of approval/ submission of the Investigational New Drug (IND) application to the date of submission of the NAS application in FDA

EMA review time
Time calculated as the difference among the approval time minus the sum of the company time and the EU commission time.

EU commission time
Time calculated from the date of end of scientific assessment to the date of approval by the EU commission.

Expedited review
Refers to EMA 'Accelerated Assessment', FDA/PMDA/Health Canada/TGA 'Priority Review' and Swissmedic 'Fast-track'.

Facilitated regulatory pathway
Regulatory pathway designed to facilitate availability, review and/or approval of medicines where there is an unmet medical need by providing alternatives to standard regulatory review routes.

Interquartile range (IQR)
The interquartile range is calculated as the difference between the 75th percentile and the 25th percentile of a distribution of measurements.

New active substances (NASs)*
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 change of name, for an existing compound (i.e., a 'cloned' application).
- Emergency use or Special authorisations derived from an emergency (e.g. COVID-19 pandemic)

*The full list of NASs approved by each jurisdiction in 2023 will be available on the CIRS website.

Real-world data (FDA definition)
Real-world data are the data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources. RWD can come from a number of sources, for example:

- Electronic health records.
- Claims and billing activities.
- Product and disease registries.
- Patient-generated data including in home-use settings.
- Data gathered from other sources that can inform on health status, such as mobile devices.

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

Time from submission to the end of Scientific Assessment

Time from submission to the end of Scientific Assessment has been defined as follows for the six agencies. It includes agency and company time and is calculated as time from acceptance of the submission for evaluation submission until:

- EMA: The CHMP issues an opinion for granting a marketing authorisation. Excluded is the time from CHMP opinion to final decision by the European Commission.
- FDA: The FDA action letter to approve is signed (FDA action date). This is equivalent to the regulatory approval, and therefore for FDA, time from acceptance of submission to end scientific assessment and time from acceptance of submission to approval are the same.
- PMDA: The First/Second Committee on New Drugs' meeting, when it is concluded that a marketing authorisation can be granted. Excluded is the time from New Drugs meeting to MHLW final decision.
- Health Canada: The last review stream is completed and the outcome letter is sent. Excluded is further time to ensure the information on file is complete and properly filed, generate drug identification numbers, prepare an executive summary and prepare the Notice of Compliance (NOC) package for routing and sign off as well as time to check that requirements are met with respect to the Patented Medicines (NOC) Regulations and the data protection provisions .
- Swissmedic: The advisory committee review and decision is made and the outcome letter (preliminary decision) is sent. Excluded is the negotiation time with the sponsor regarding the label following the end of the scientific review.
- TGA: The delegate decision is made and the decision (outcome letter) is sent to the sponsor. This is equivalent to the regulatory approval, and therefore for TGA, time from acceptance of submission to end scientific assessment and time from acceptance of submission to approval are the same.

Top company

Pharmaceutical company with R&D spending >3 billion USD in 2020.

World Health Organisation (WHO) ATC classification

- A - Alimentary and metabolism: Drugs for acid related disorders, gastrointestinal disorders, antiemetics and antinauseants, bile and liver therapy, laxatives, antidiarrheals, intestinal antiinflammatory/antiinfective agents, drugs used in diabetes.
- B – Blood and blood forming organs: antithrombotic agents, antihemorrhagics, antianemic preparations, blood substitutes and perfusion solutions, other hematological agents.
- J - Anti-infectives: Antibacterials for systemic use, antimycotics for systemic use, antimycobacterials, antivirals for systemic use, immune sera and immunoglobulins, vaccines.
- L - Anticancer and immunomodulators: Antineoplastic agents, endocrine therapy, immunostimulants, immunosuppressive agents.
- N - Nervous system: Anesthetics, analgesics, antiepileptics, anti-parkinson drugs, psycholeptics, psychoanaleptics, other nervous system.

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About CIRS

The Centre for Innovation in Regulatory Science (CIRS) is a neutral, independent UK-based subsidiary of Clarivate plc. CIRS provides an international forum for industry, regulators, health technology assessment (HTA) and other healthcare stakeholders to meet, debate and develop regulatory and reimbursement policy through the innovative application of regulatory science. 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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