New drug approvals in six major authorities 2012-2021:

Focus on facilitated regulatory pathways and internationalisation

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 2021 as well as looking back at 2012-2021. Although median approval times can be a marker of agency performance and the time it takes to make medicines available to patients, other factors need to be taken into account. This R&D Briefing focuses on factors such as facilitated regulatory pathways (FRPs), internationalisation of NASs, as well as the use of novel data sources, including real-world data (RWD).

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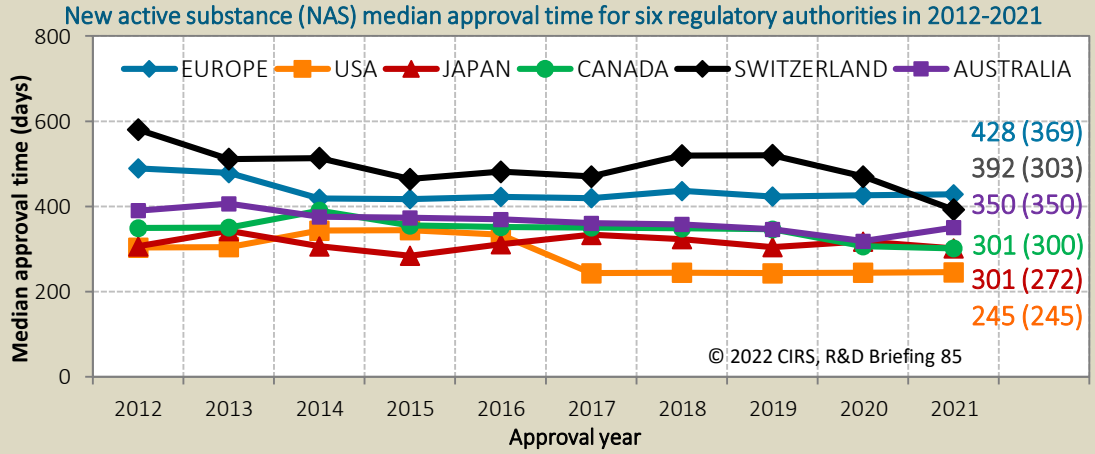
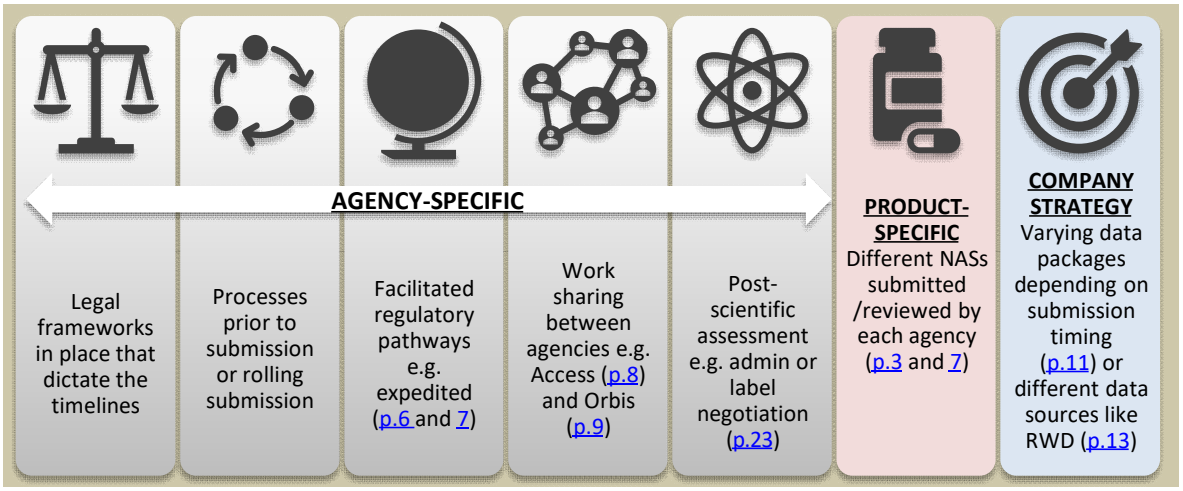
New active substance (NAS) median approval time for six regulatory authorities in 2012-2021



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 2021; (N2) = median time from submission to the end of scientific assessment (see p.23) for products approved in 2021.

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



Key messages

- In 2021, FDA (Centre for Drug Evaluation and Research, CDER, and Centre for Biologics Evaluation and Research, CBER, combined) approved the highest number of NASs (52) (Fig. 1). The **overall number of NASs approved by the six agencies has generally increased** from 2012 to 2021, however, for FDA and Health Canada it has flattened over the past five years.
- In 2021, FDA had the shortest **median approval time** (245 days), which is likely due to the wide use of FRPs. This was followed by Health Canada and PMDA (301 days for both agencies), TGA (350 days), Swissmedic (392 days) and EMA (428 days) (Fig. 2).
- All six agencies offer an **expedited process** designed to hasten the review process of promising NASs (Fig. 3). In 2021, the ratio of expedited approvals to standard reviews was highest for FDA (71%), followed by PMDA (45%), Health Canada (26%), TGA (14%), EMA (9%) and Swissmedic (8%).
- EMA was the agency with the greatest difference in **median approval time between expedited and standard** review in 2021, with a difference of 184 days, whereas the smallest difference was for PMDA, with 65 days. The difference between standard and expedited review was 154 days for Swissmedic, 136 for Health Canada, 133 for TGA and 123 for FDA (Fig. 4).
- In 2021, **the proportion of approved NASs with an orphan designation was high** across the agencies with 40% for TGA, 36% for EMA, 42% for PMDA, 49% for Swissmedic and 54% for FDA (Fig.5).
- Over the last five years (2017-2021), the **usage of facilitated regulatory pathways (FRPs) has increased** for most of the agencies compared with the beginning of the decade (2012-2016) (Fig. 7). Meanwhile, the **number of conditional/accelerated/provisional approvals has gone up** in the last five years for all agencies (Fig. 8).
- For all assessed agencies, **median submission gap and median approval time were faster for NASs approved via Access Consortium** compared to all NASs approved between 2018 and 2021 (Fig. 11), suggesting that worksharing is having a positive impact on the roll out time (submission gap + approval time).
- The **median roll out times were shortened** for the agencies where comparisons could be made **when comparing Orbis approvals to other anti-cancer and immunomodulator approvals** (Fig. 13), thereby demonstrating that global regulatory collaboration is attainable and can deliver faster access to new therapies for patients with cancer.
- The **top five therapeutic areas** (TAs) by number of NASs approved across all six agencies made up 77% (821/1060) of all approvals between 2017-2021, with anti-cancer and immunomodulators making up 53% (433) of the top five TAs approvals (Fig. 14).
- **The number of products approved by all six agencies in a five-year period** decreased from 56 NASs in 2012-2016 to 43 NASs in 2017-2021, compared to analyses in the past years where there was an increase (see R&D Briefing 70, 77, 81), suggesting that the pace of internationalisation may be levelling off (Fig. 16).
- The **variance in company submission strategy was further analysed by comparing the distribution in submission gap** for NASs approved by all six agencies in 2012-2016 (56) with 2017-2021 (43). This shows that median submission gap of PMDA decreased from one year in 2012-2016 to approximately half a year in 2017-2021 (Fig.17) .
- The **inclusion of RWD as part of the application was analysed for EMA and FDA for 2021**. For EMA, 24% of approvals included RWD, compared to 33% for FDA (Fig. 19)

See agency-specific infographics for 2021 snapshots:

EMA	FDA	PMDA	Health Canada	Swissmedic	TGA
p.15	p.16	p.17	p.18	p.19	p.20

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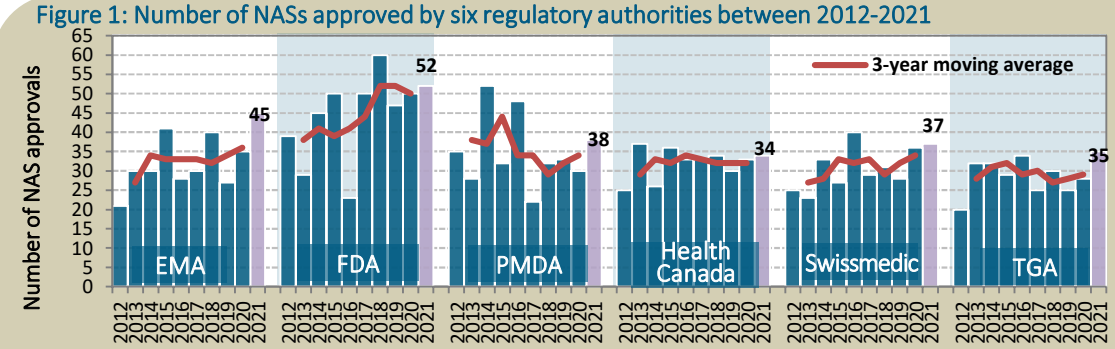
Overall approvals

Figure 1: Number of NASs approved by six regulatory authorities between 2012-2021



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In 2021, FDA (Centre for Drug Evaluation and Research, CDER, and Centre for Biologics Evaluation and Research, CBER, combined) approved the highest number of NASs (52) (Fig. 1). The overall number of NASs approved by the six agencies has generally increased from 2012 to 2021, however, for FDA and Health Canada it has flattened over the past five years. The rationale for the typically higher number of approvals by FDA compared to other agencies may be the availability of FRPs, or that some of the medicines approved by FDA, particularly from smaller companies, do not become internationalised. Comparing the number of NAS approvals during the two halves of the decade, 2012-2016 and 2017-2021, revealed that the biggest change was seen for FDA, with a 39% increase, followed by EMA (18%), Swissmedic (9%), and Health Canada (4%), whereas the number of TGA and PMDA approvals decreased by 3% and 21% respectively. The variance in the number of products approved by each agency may be explained by a number of factors, such as different submission strategies to each agency, depending on company size, unmet medical need and review speed.

Figure 2: NAS approval time for six regulatory authorities between 2012-2021

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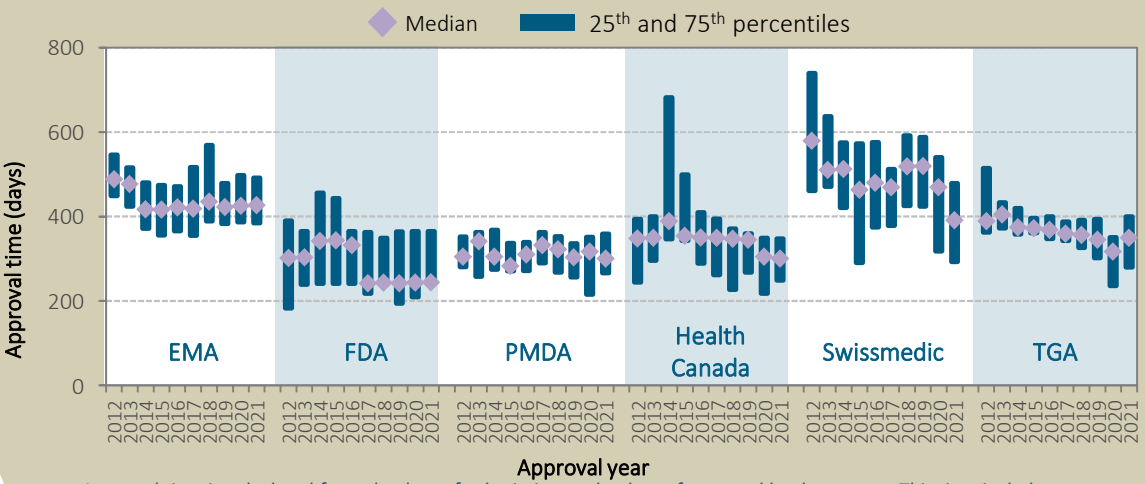
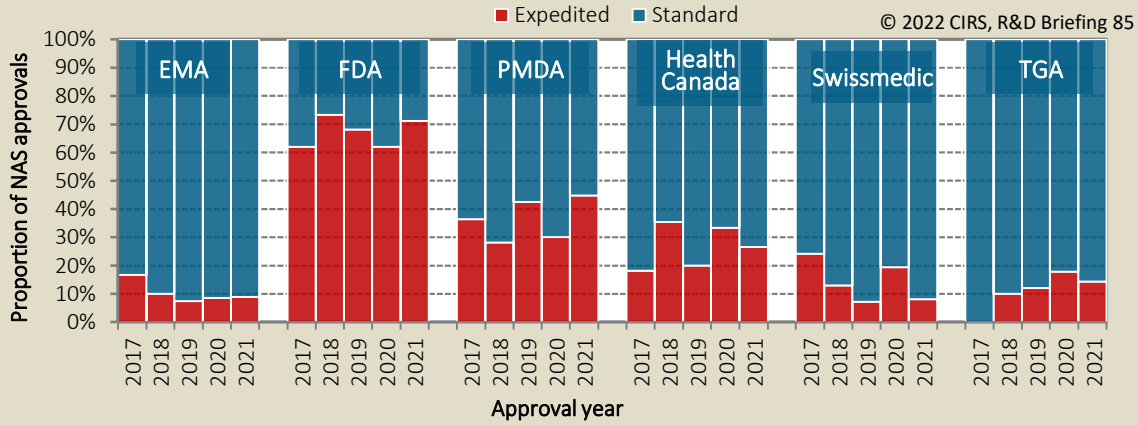


Approval time is calculated from the date of submission to the date of approval by the agency. This time includes agency and company time. EMA approval time includes the EU Commission time.

In 2021, FDA had the shortest median approval time (245 days), which is likely due to the wide use of FRPs. This was followed by Health Canada and PMDA (301 days for both agencies), TGA (350 days), Swissmedic (392 days) and EMA (428 days) (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; 183 days between FDA and EMA). However, this difference was a narrower when comparing the median time from submission to the end of scientific assessment (124 days between FDA and EMA). For FDA, Health Canada and TGA, the overall approval time and the time to end of scientific assessment were the same or similar, which indicates that very few activities or no time-consuming activities occur after the scientific assessment. The biggest difference in median approval time between 2020 and 2021 was for Swissmedic, where it decreased by 78 days, mainly as a result of the decrease in time following scientific assessment (e.g. for label negotiation), where this was 173 days in 2020 compared to 89 in 2021. In 2021, TGA approval times were longer compared to 2020 which may be as result of increased workload due to the COVID-19 pandemic.

Characteristics: Review type

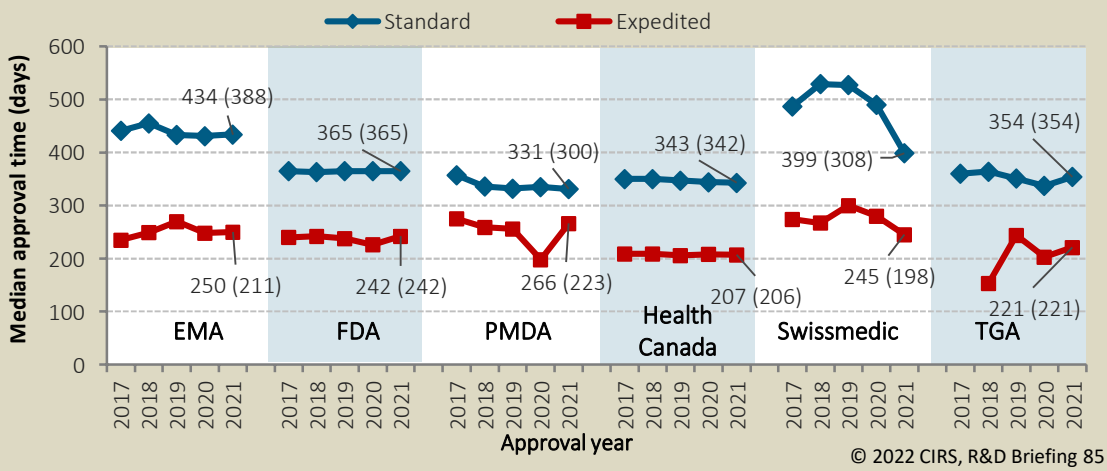
Figure 3: Number of NAS approvals by review type for six regulatory authorities between 2017-2021



'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. 3). In 2021, the ratio of expedited approvals to standard reviews was highest for FDA (71%), followed by PMDA (45%), Health Canada (26%), TGA (14%), EMA (9%) and Swissmedic (8%). TGA implemented its priority system in 2017; three expedited approvals were granted in 2018, another three in 2019, and five for each year in 2020 and 2021. The proportion of expedited approvals has been consistently high for FDA and increased from 50% between 2012-2016 (results not shown) to 68% between 2017-2021. Swissmedic had three expedited approvals in the last year, followed by EMA with four. With respect to EMA, this is partially because the review type can be reverted to standard review if timelines cannot be met by the sponsor. For instance, in 2021, nine NASs initially designated by EMA as expedited were reverted, whereas for seven NASs, the applicant requested expedited review, but EMA did not agree.

Figure 4: NAS median approval time by review type for six regulatory authorities between 2017-2021

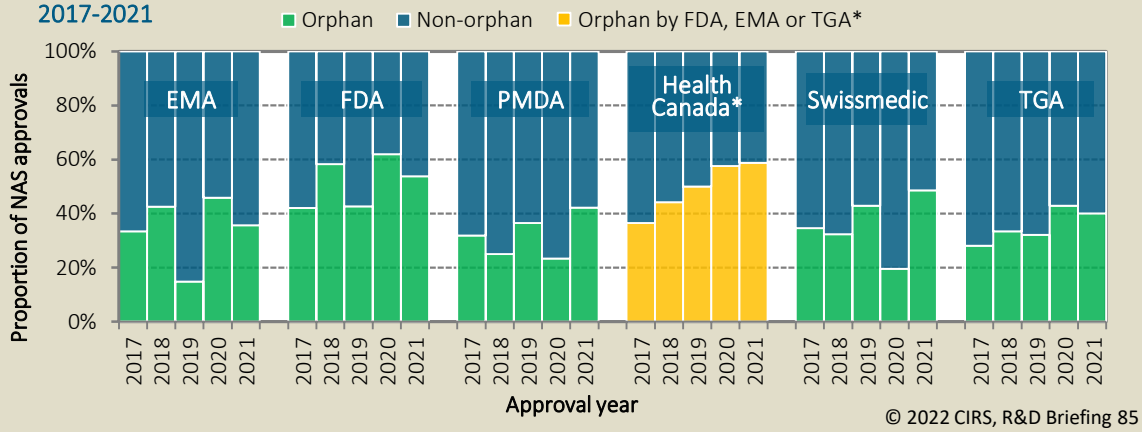


'Expedited review' refers to EMA 'Accelerated Assessment', Swissmedic 'Fast Track' and FDA/PMDA/Health Canada/TGA 'Priority Review'. TGA introduced an expedited (priority) review programme in 2017. Approval time is calculated from the date of submission to the date of approval by the agency. This time includes agency and company time. EMA approval time includes the EU Commission time. N1 = overall approval time for 2021; (N2) = time from submission until the end of scientific assessment (see p.23) for 2021.

EMA was the agency with the greatest difference in median approval time between expedited and standard review in 2021, with a difference of 184 days, whereas the smallest difference was for PMDA, with 65 days. The difference between standard and expedited review was 154 days for Swissmedic, 136 for Health Canada, 133 for TGA and 123 for FDA. Interestingly, for Swissmedic, the additional label negotiation activities taking place following the end of scientific assessment were taking approximately half the time for products designated as expedited compared to standard, demonstrating that label negotiations and other administrative activities are being carried out more quickly for high unmet need products. Finally, in 2021, the median review time for the five products approved through the introduced expedited pathway by TGA was 221 days, which is in line with the other agencies.

Characteristics: Orphan designation

Figure 5: Proportion of NAS approvals by orphan designation for six regulatory authorities between 2017-2021

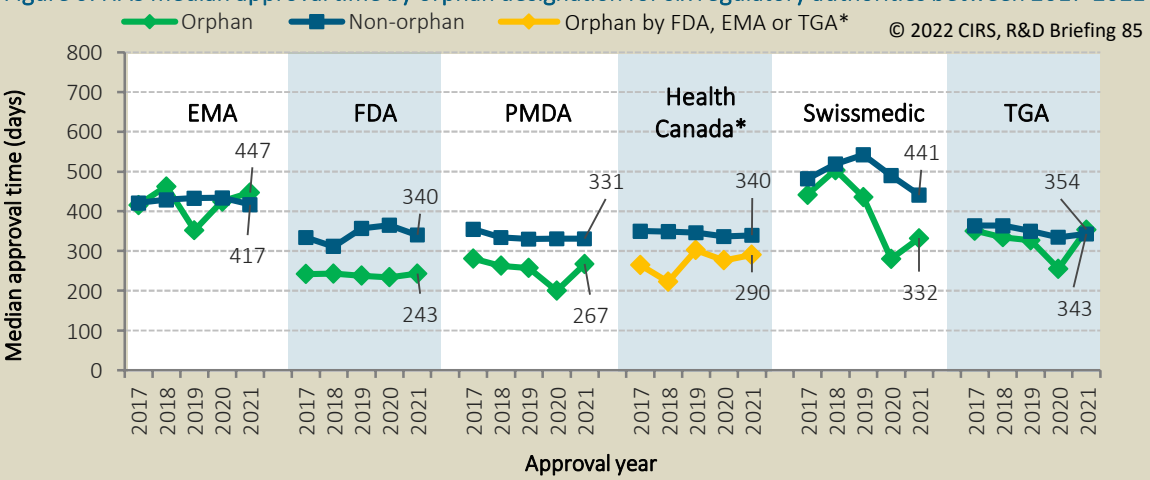


** Health Canada does not currently have an orphan policy; this data shows the number of medicines that were approved by Health Canada that were classified as orphan by either FDA, EMA or TGA.*

In 2021, the proportion of approved NASs with an orphan designation was high across the agencies with 40% for TGA, 36% for EMA, 42% for PMDA, 49% for Swissmedic and 54% for FDA (Fig.5). Although Health Canada does not currently have an orphan policy, 59% of the NASs approved by the agency in 2021 were classified as orphan by either FDA, EMA or TGA.

From 2017-2021, the proportion of orphans varied year-on-year but has generally increased between for each agency. This may be due to disease stratification and companies' growing R&D pipelines and is consistent with increased commitment from agencies to tackle unmet medical needs. The variance across agencies may be due to the types of products submitted to each agency as well as differences in orphan designation criteria across the agencies, or the indication submitted by the sponsor.

Figure 6: NAS median approval time by orphan designation for six regulatory authorities between 2017-2021



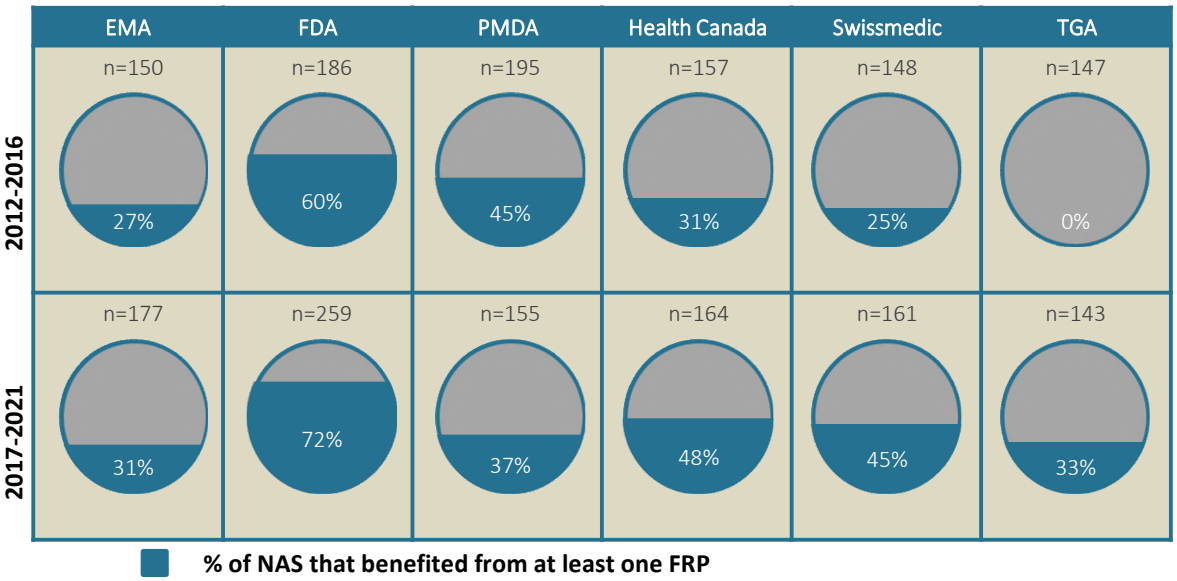
Approval time is calculated from the date of submission to the date of approval by the agency. This time includes agency and company time. EMA approval time includes the EU Commission time.
**Health Canada does not currently have an orphan policy; this data shows the number of medicines that were approved 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 2017-2021 (Fig. 6). FDA had the fastest median approval time for orphans in 2021 (243 days), as most of these products were approved through expedited review. PMDA had the second fastest median approval time for orphans in 2021 (267 days). All orphan NASs approved in Japan went through expedited review, due to an incentive from PMDA to address unmet needs. Health Canada does not currently have an orphan policy; however, for the 20 NASs approved by Health Canada in 2021 that were classified as orphan by either FDA, EMA or TGA, the median approval time was 290 days. For the 16 orphans approved by EMA in 2021, the median approval time was 447 days, where 13% of the orphans were expedited by the agency whereas in 2019, 50% of the orphans were expedited with a median approval time of 352 days for the four orphans approved in that year.

Characteristics: Facilitated regulatory pathways (FRPs)

Over the last five years (2017-2021), the usage of facilitated regulatory pathways (FRPs) has increased for most of the agencies compared with the beginning of the decade (2012-2016). FDA was the agency that mostly used FRPs with 72% of NASs that had at least one FRP, followed by Health Canada (48%), Swissmedic (45%), PMDA (37%), TGA (33%) and EMA (31%). TGA was the agency that has seen the biggest increase in the number of NAS approvals with FRPs, which demonstrates the recent implementation of the five FRPs by TGA (Priority review, Provisional approvals, Comparable overseas regulators (COR) review, Access Worksharing Consortium, and Project Orbis). PMDA was the only agency where the proportion of NASs approved with an FRP decreased slightly when comparing 2012-2016 versus 2017-2021.

Figure 7: Proportion of NAS approved by each agency between 2012-2016 vs 2017-2021 that benefited from an FRP



The number of conditional/accelerated/provisional approvals has generally gone up in the last five years acoss the six agencies. FDA was the agency that approved the most NASs using these pathways in 2017-2021, with 47 approvals, followed by EMA (30), Health Canada (28), Swissmedic (15), TGA (13) and PMDA (3). Furthermore, the number of NASs approved via these pathways has generally been increasing year on year across the six agencies and was highest in 2020 and 2021, which may be due to COVID-19 related products.

Figure 8: Number of NAS approved through a conditional/accelerated/provisional approval pathway by the six major authorities between 2017-2021

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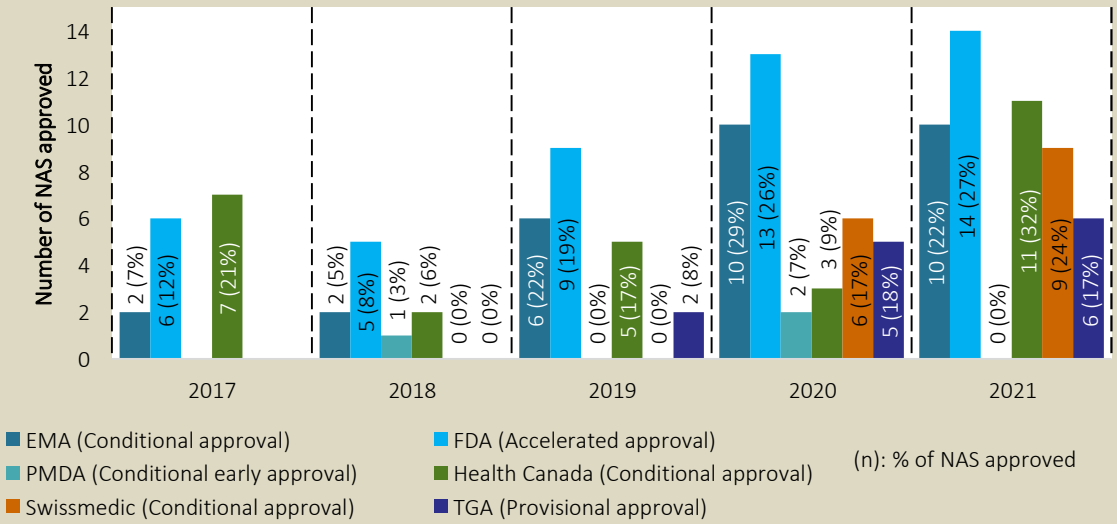
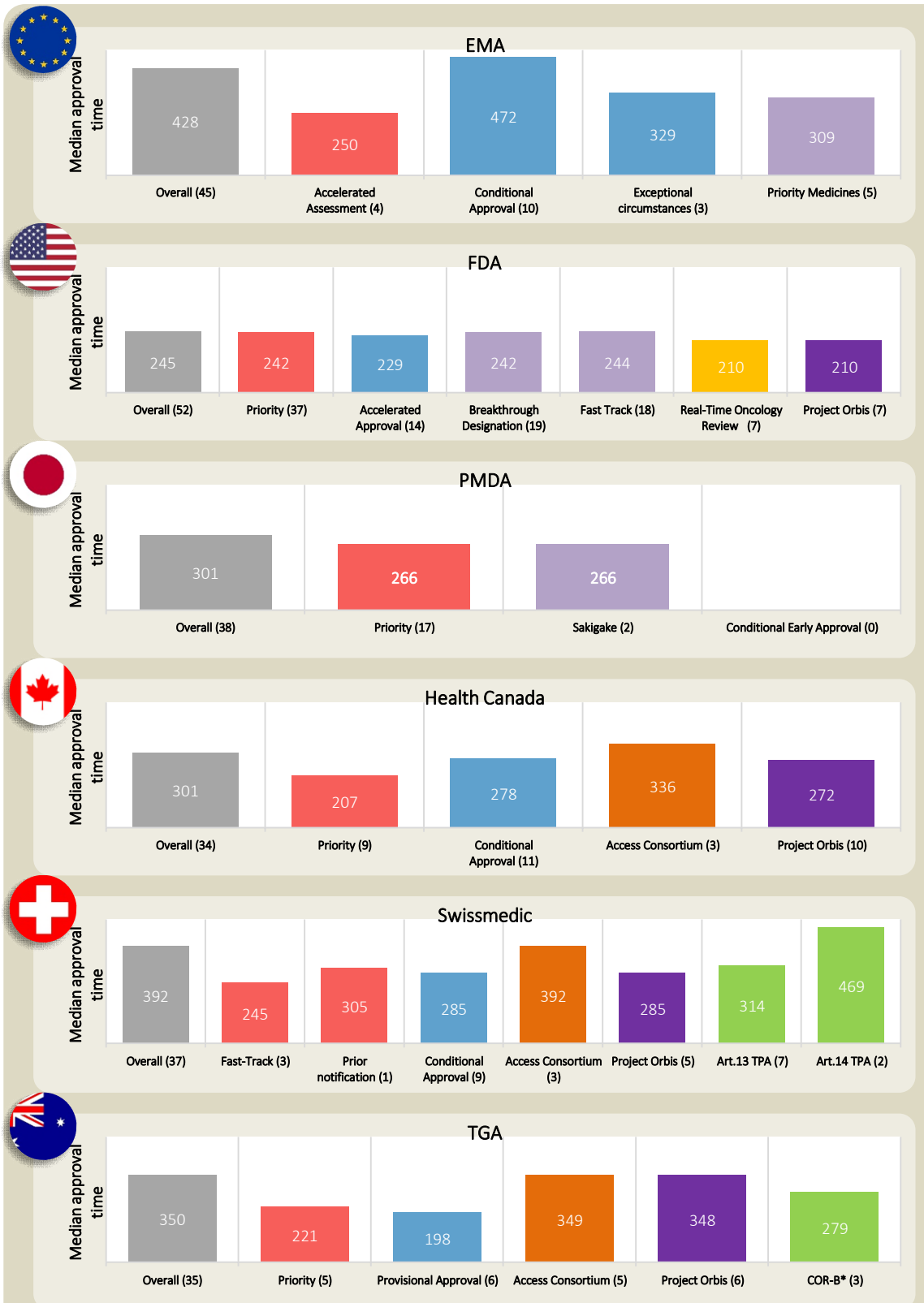


The 2021 NAS median approval times for the different FRPs are illustrated on the next page (Fig. 9).

Characteristics: Facilitated regulatory pathways (FRPs)

Figure 9: Facilitated regulatory pathway (FRP) timelines across six agencies; focus on 2021



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(n) = number of NASs

- Expedited review
- Conditional/accelerated/provisional approvals
- Earlier/ Intensive dialogue review
- Real time review
- Work-sharing review
- Collaborative review
- Reliance/abridged/simplified review

** COR-B: Comparable overseas regulators (COR) review Type B is a shortened decision timeframe (175 working days) evaluation for prescription medicines that have already been approved by a COR partner. For more FRP definitions go to p.21 and 22 of this R&D Briefing.*

Focus: Access Worksharing Consortium

The Access Consortium is a medium-sized coalition, which was formed in 2007 by 'like-minded' regulatory agencies to promote greater collaboration and alignment of regulatory requirements. Its goal is to maximise international cooperation, reduce duplication, and increase each agency's capacity ensuring timely access to high quality, safe and effective medicines to patients. As part of the work-sharing process, the agencies review different parts of the dossier. Although the review is shared, each regulator makes an independent decision regarding approval (market authorisation) of the new medicine. This model of work-sharing is being watched to see if this could be a model for other like-minded agencies to share resource both within and across regions and to streamline company interactions. NAS approvals for 2018-2021 were analysed across Health Canada, Swissmedic, TGA and the Singaporean Health Sciences Authority (HSA) as part of the New Chemical Entities Work Sharing Initiative, where 12 NASs were approved in total across the agencies. TGA was the agency that participated the most in the worksharing with all 12 NASs, mostly anti-cancer and immunomodulators (Fig.10), followed by Health Canada (9), HSA (4) and Swissmedic (4). In January 2021, the UK Medicines and Healthcare products Regulatory Agency (MHRA) started work-sharing applications within this initiative, however no NASs were approved in that year.

Figure 10: Number of NAS approved through the Access Consortium between 2018-2021 by type of therapeutic indication

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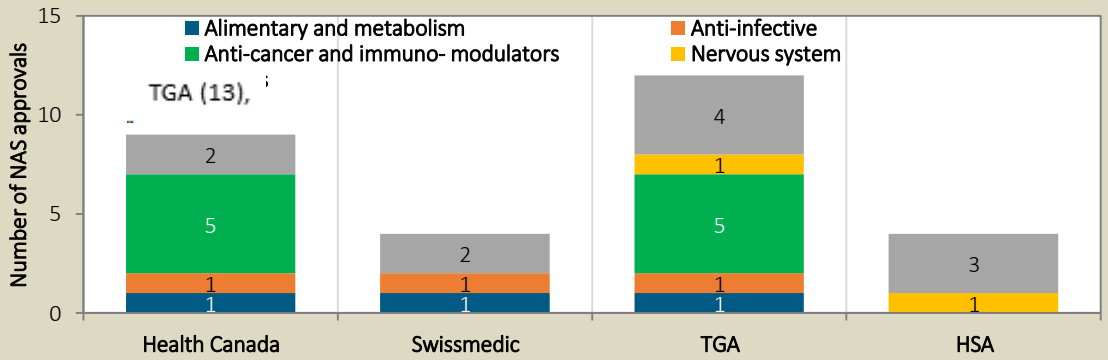

For all assessed agencies, median submission gap and median approval time were faster for NASs approved via Access Consortium compared to all NASs approved between 2018 and 2021 (Fig. 11), suggesting that worksharing is having a positive impact on the roll out time (submission gap + approval time). In terms of overall median roll out time, this was 326 days faster for Swissmedic for Access NASs compared to all NASs approved between 2018 and 2021, followed by HSA with 225 days, TGA with 224 days and Health Canada with 220 days.

Figure 11: Median submission gap and median approval time for all NASs approved compared to those approved via the Access Consortium between 2018-2021

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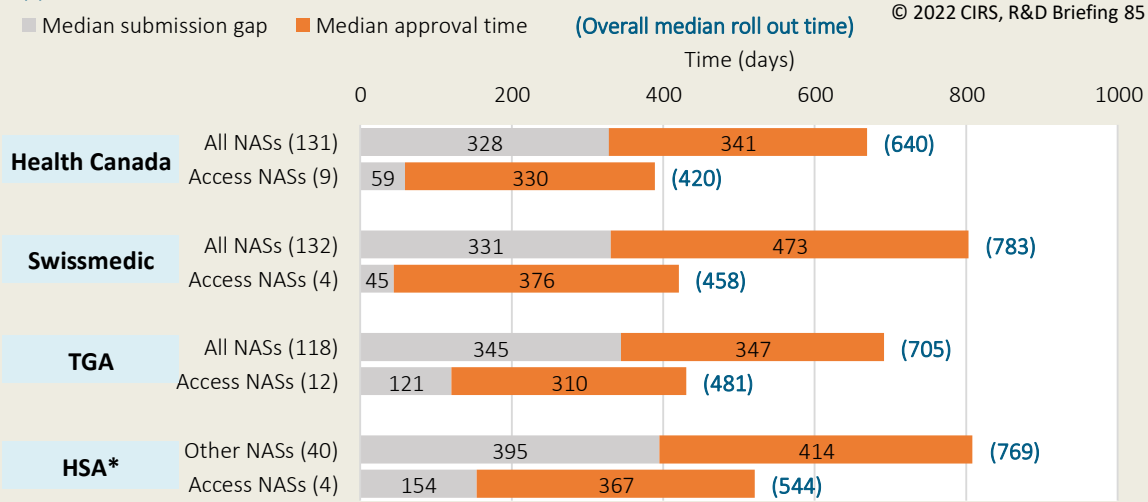
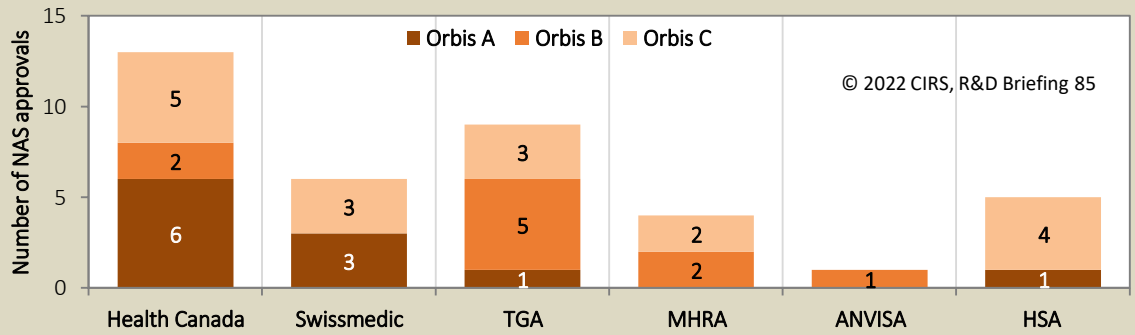


(N) = number of approvals
Submission gap is calculated as the time from date of submission at the first regulatory agency to the date of regulatory submission to the target agency. Approval time is calculated from the date of submission to the date of approval by the agency. This time includes agency and company time. Roll out time is calculated from date of submission at the first regulatory agency to the date of regulatory approval at the target agency.
**For HSA, the timelines for other NASs were obtained from Industry – CIRS Emerging Markets Programme, 2019-2021 approval.*

Focus: Project Orbis

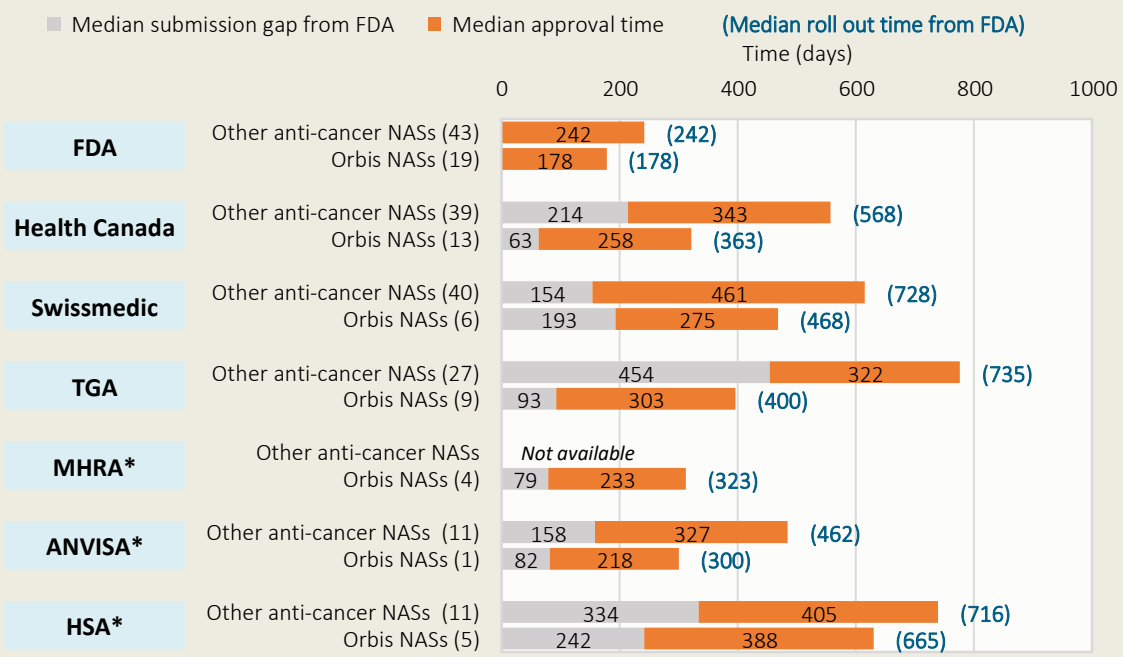
Project Orbis is an initiative of the US FDA Oncology Center of Excellence that aims to give patients faster access to promising cancer treatments across the globe. Project Orbis partners work together on the review of submissions for cancer drugs. There are three types of Project Orbis submissions which are dependent on the timelines between FDA and partners: A, where submission is largely concurrent, compared to B, where there is a >30 day delay from FDA to partner submission, or C, where submission occurs once FDA has already taken regulatory action. For NASs approved through Project Orbis between 2019-2021 (Fig.12), the highest number was by Health Canada (13), most being Orbis A, followed by TGA (9), Swissmedic (6), HSA (5), MHRA (4) and the Brazilian Health Regulatory Agency ANVISA (1). The most commonly used Orbis type was C, suggesting that the most frequent experience is for FDA to share their completed review documents without a concurrent review.

Figure 12: Number of NASs approved through Project Orbis by agency between 2019-2021, by Orbis Type



The median roll out times from FDA were shortened when comparing Orbis approvals to other anti-cancer and immunomodulator approvals based on shorter submission gap from FDA and approval time (Fig. 13), thereby demonstrating that global regulatory collaboration is attainable and can deliver faster access to new therapies for patients with cancer.

Figure 13: Median submission gap from FDA and median approval time for non-Orbis anti-cancer and immunomodulator NASs (ATC=L) compared to those approved via Project Orbis between 2019-2021



(N) = number of approvals

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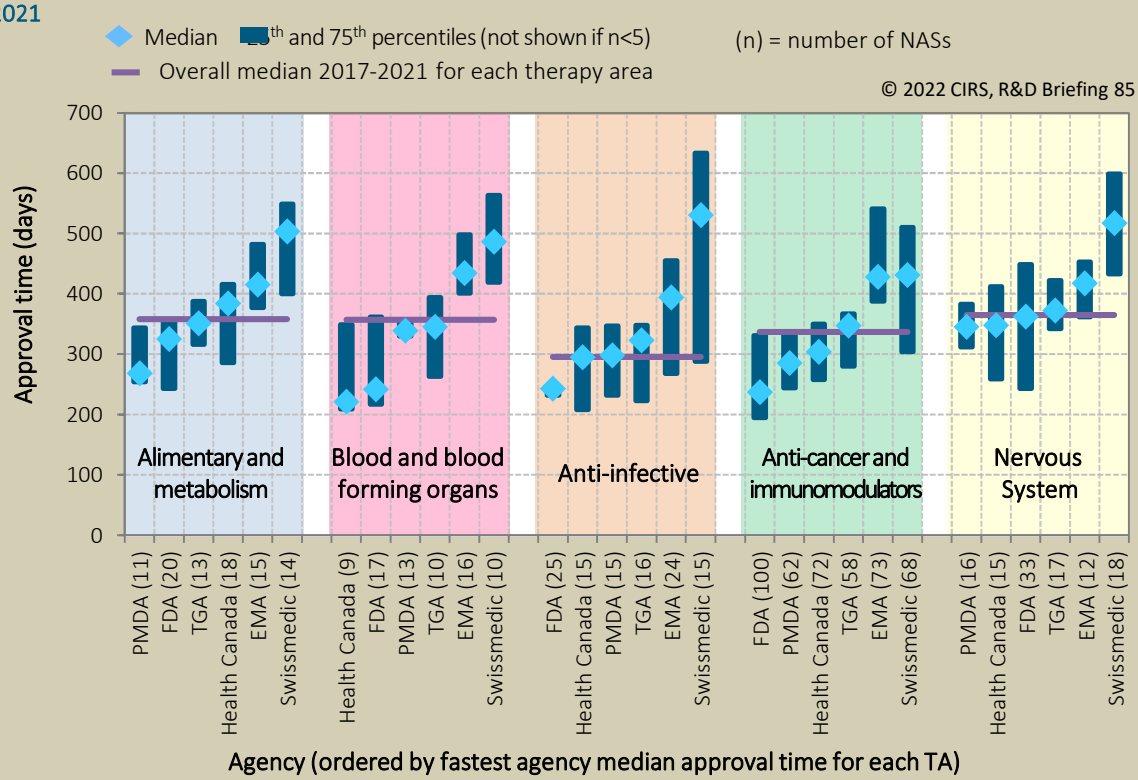
Submission gap from FDA is calculated as the time from date of submission at FDA to the date of regulatory submission to the target agency. Approval time is calculated from the date of submission to the date of approval by the agency. This time includes agency and company time. Roll out from FDA is calculated from date of submission at FDA to the date of regulatory approval at the target agency.

** For ANVISA and HSA, the timelines for other anti-cancer and immunomodulator NASs were obtained from Industry – CIRS Emerging Markets Programme, 2019-2021 approval, and for Orbis NASs they were obtained from the agency website and the agency directly for ANVISA and HSA respectively. For MHRA, the submission dates were obtained directly from the companies.*

Characteristics: Therapeutic area

Figure 14: NAS median approval time by top five therapeutic areas (TA) for six regulatory authorities between 2017-2021



Therapy areas relate to the WHO ATC codes. 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.

The top five TAs by number of NASs approved across all six agencies made up 77% (821/1060) of all approvals between 2017-2021, with anti-cancer and immunomodulators making up 53% (433) of the top five TAs approvals (Fig. 14). Anti-infective therapies were approved marginally faster with an overall median approval time of 296 days, compared with 337 days for anti-cancer and immunomodulators and 357 for blood and blood forming organs therapies, 358 days for alimentary and metabolism and 365 days for nervous system NASs. PMDA was the fastest for alimentary and metabolism, as well as nervous system areas, whereas FDA was the fastest for anti-cancer and immuno-modulators as well as anti-infectives. This may reflect the more frequent use of expedited review pathways by agencies across the five therapy areas (Fig. 15). Nevertheless, as noted by the 25th-75th percentile bars, there were also wide variations for certain jurisdictions across therapy areas.

Figure 15: NAS overall median approval time by top five therapeutic areas in relation to expedited approvals for six regulatory authorities between 2017-2021

© 2022 CIRS, R&D Briefing 85	Alimentary and metabolism		Blood and blood forming organs		Anti-infective		Anti-cancer and immuno-modulators		Nervous system	
Approval time, days (proportion of expedited approvals)										
EMA	415	(27%)	434	(19%)	394	(8%)	428	(5%)	417	(17%)
FDA	325	(65%)	242	(65%)	243	(92%)	237	(77%)	362	(45%)
PMDA	268	(55%)	339	(31%)	298	(53%)	285	(52%)	345	(6%)
Health Canada	384	(22%)	221	(56%)	295	(40%)	304	(22%)	348	(33%)
Swissmedic	503	(0%)	486	(0%)	530	(20%)	431	(19%)	517	(11%)
TGA	351	(8%)	345	(20%)	323	(0%)	347	(12%)	372	(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'. TGA introduced an expedited (priority) review programme in 2017, therefore the numbers in parentheses only relate approvals from 2018 to 2021. 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.

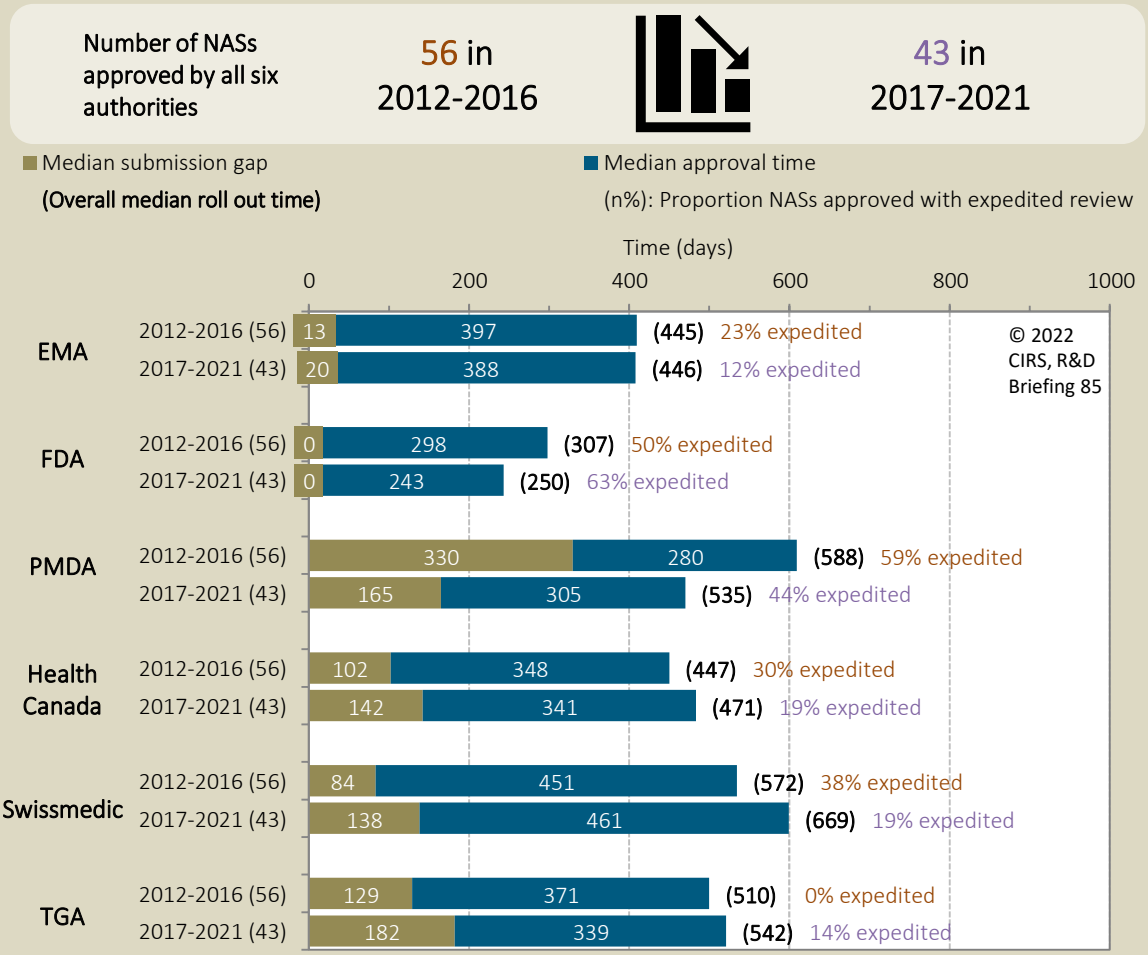
Common approvals across the six regulatory agencies

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 the two time cohorts in the last decade (2012-2016 and 2017-2021) to identify trends. The number of products approved by all six agencies in a five-year period decreased from 56 NASs in 2012-2016 to 43 NASs in 2017-2021, compared to analyses in the past years where there was an increase (see R&D Briefing 70, 77, 81), suggesting that the pace of internationalisation may be levelling off.

The roll out time, consisting of the submission gap and approval time (Fig. 16), can be influenced by a number of factors such as company submission strategy and the use of expedited pathways to address unmet medical need. The fastest overall median roll out time for the 2017-2021 cohort was for FDA with 250 days, as a result of companies submitting there first and quick regulatory review times due the wider use of expedited reviews (63%), followed by EMA with 446 days, Health Canada with 471 days, PMDA with 535 days, TGA with 542 days and Swissmedic with 669 days.

Submission to EMA occurred almost simultaneously with FDA, followed by Health Canada, Swissmedic, TGA and PMDA. 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 was halved from 330 days in 2012-2016 to 165 days in 2017-2021.

Figure 16: Median submission gap and median approval time for NASs approved by all six authorities in 2012-2016 (56) compared with 2017-2021 (43), as well as the proportion of NASs approved as expedited

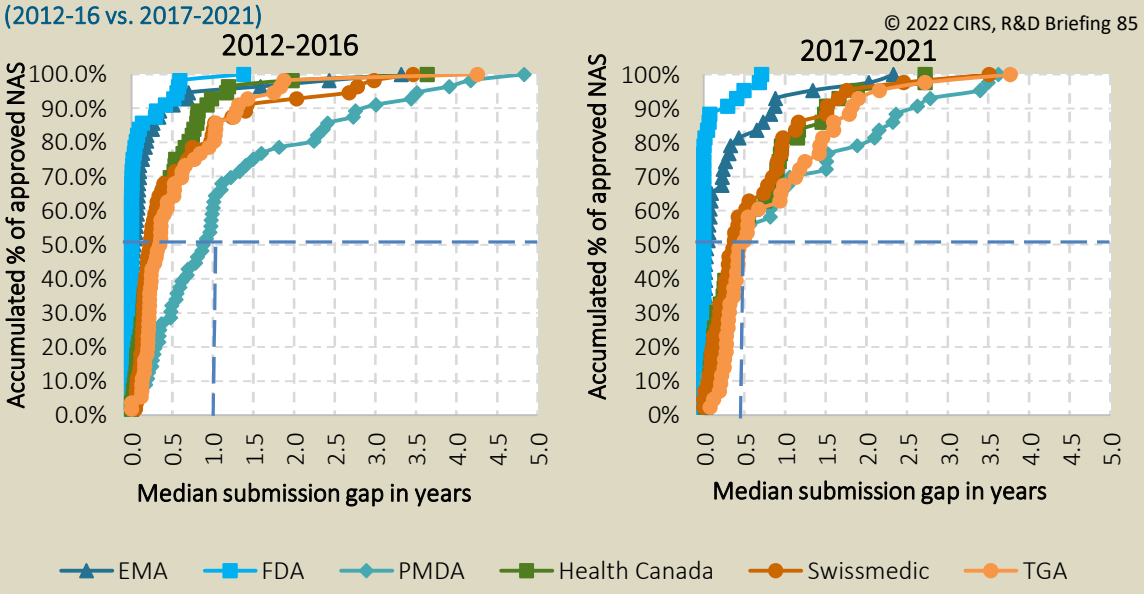


Submission gap is calculated as the time from date of submission at the first regulatory agency to the date of regulatory submission to the target agency. Expedited review' refers to EMA 'Accelerated Assessment', Swissmedic 'Fast Track' and FDA/PMDA/Health Canada/TGA 'Priority Review'. TGA introduced an expedited (priority) review programme in 2017, therefore the numbers for 2017-2021 only relate to 2018-2021 approvals. 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.

Common approvals across the six regulatory agencies

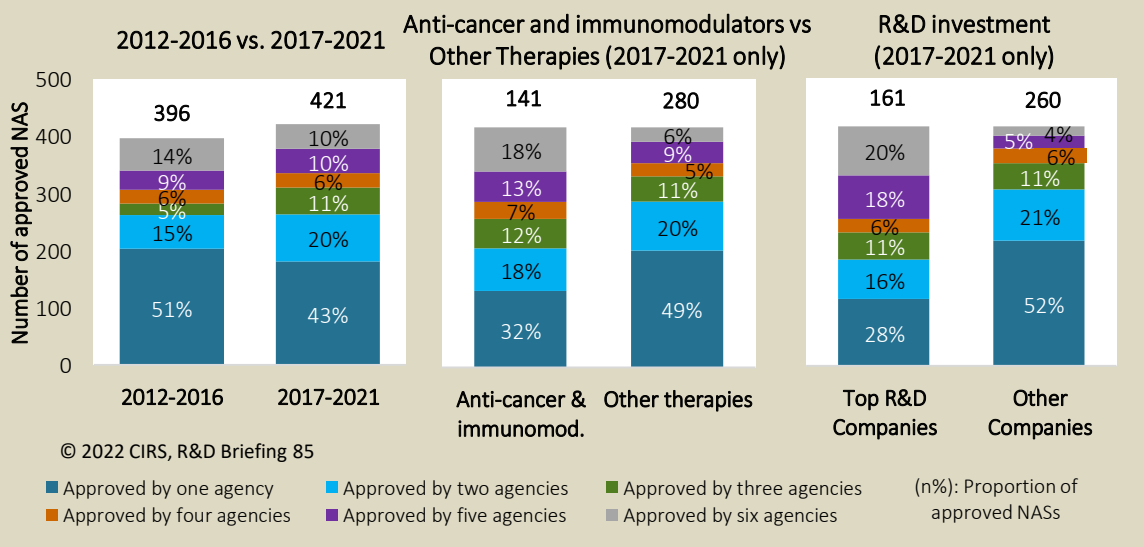
The variance in company submission strategy was further analysed by comparing the distribution in submission gap for NASs approved by all six agencies in 2012-2016 (56) with 2017-2021 (43). This shows that median submission gap for PMDA decreased from one year in 2012-2016 to approximately half a year in 2017-2021 (Fig.17) . The tightening of the distribution curve for PMDA in the 2017-2021 cohort suggests that time taken to submit to PMDA following first world submission is now similar to that for Health Canada, Swissmedic and TGA.

Figure 17: First world submission to agency submission time analysis for NASs approved in all agencies (2012-16 vs. 2017-2021)



The internationalisation of products was studied by comparing the number of agencies that approved each NAS. A comparison of 2012-2016 and 2017-2021 demonstrated that although the number of products approved by all six agencies did not increase as was observed in previous years, the proportion of NASs approved by two or more agencies increased from 49% in 2012-2016 to 57% in 2017-2021. Possible factors that impact internationalisation were explored for 2017-2021. The biggest differences were seen when comparing therapy area and company size based on R&D spend. For therapy area, 18% of anti-cancer and immunomodulator NASs were approved by all six agencies, compared to 6% for other therapy areas. With respect to R&D investment levels, 20% of NASs from top companies (pharmaceutical company with R&D spending >3 billion USD in 2021) were approved by all six agencies compared to 4% of NASs from other smaller companies.

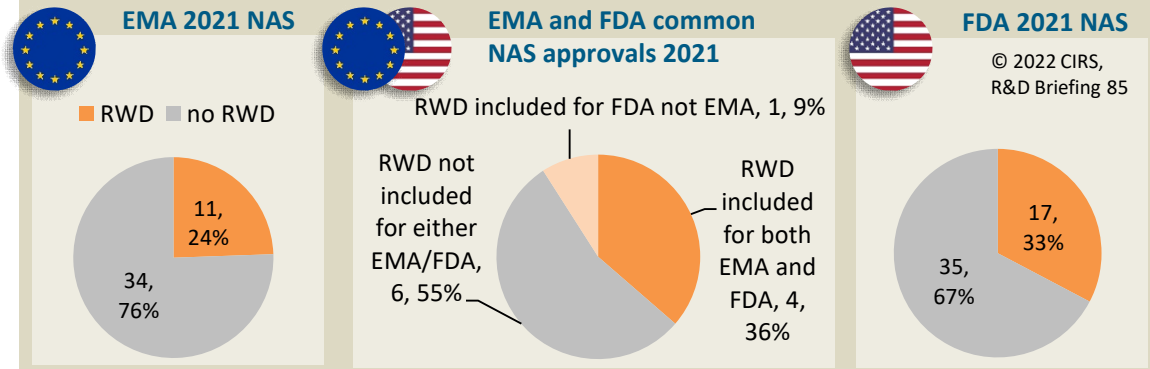
Figure 18: Number of NASs approved by one to six of the major regulatory authorities



Focus: Novel data sources

Evidence sources are changing as the regulatory landscape evolves. These changes include the increased use of real-world data (RWD) within an application and the collection and use of patient experience data (PED). This page looks at these two areas for 2021 NAS approvals. The inclusion of RWD as part of the application was analysed for EMA and FDA for 2021. For EMA, 24% of approvals included RWD, compared to 33% for FDA. RWD are the data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources, for example, from electronic health records. In 2021, there were 11 NASs approved by both EMA and FDA (Fig. 19); RWD was included for both agencies in four of these approvals, not included in six, and in the remaining case, RWD was included for FDA but not EMA. The NASs were primarily anti-cancer and immunomodulators (ATC=L), came from top companies and benefited from a number of FRPs, such as conditional for EMA and expedited (priority) for FDA.

Figure 19: Inclusion of real-world data (RWD) for NASs approved by EMA and/or FDA in 2021



EMA characteristics of RWD NAS (11)

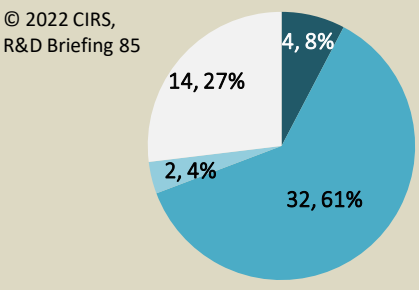
Median approval time (days)	428
ATC majority	(L)
Top company	
Orphan	
Expedited	
PRIME	
Exceptional	
Conditional	

FDA characteristics of RWD NAS (17)

Median approval time (days)	243
ATC majority	(L)
Top company	
Orphan	
Expedited	
Breakthrough	
Fast track	
Accelerated	
RTOR	

PED refers to the systematic collection of meaningful data relating to the experiences, perspectives, needs, and priorities of patients. In 2021 (Fig. 20), 52 NASs were approved by FDA, 38 out of 52 reported using PED, of which 36 out of 38 had PED submitted by the sponsor; four out of 36 the agency considered additional PED not submitted by the sponsor as part of the review. For two out of 38 NASs, although no PED had been submitted in the application, the reviewer did include other PED as part of the review.

Figure 20: Inclusion of patient experience data (PED) for 2021 FDA NAS approvals



	PED submitted by the sponsor (n=36)	No PED submitted by the sponsor (n=16)
Median approval time (days)	245	244
Median development time (days)	2128	2725
ATC majority	L (17)	L (7)
Top company	16	4
Expedited	26	11
Breakthrough	16	3
Fast track	10	4
Accelerated	12	6
RTOR	5	2

Summary of NAS approved in 2021 by the six agencies

This table summarises approval times for NAS approved in 2021 by the six agencies, broken down by product type, review type and major therapeutic area.

Agency median time in calendar days	EMA  p.16	FDA  p.17	PMDA  p.18	Health Canada  p.19	Swissmedic  p.20	TGA  p.21
Number of NAS approved	45	52	38	34	37	35
NAS overall approval time (days)	428	245	301	301	392	350
By biologics (days)	399	335	276	272	374	330
By chemicals (days)	451	243	329	301	410	356
By standard review (days)	434	365	331	343	399	354
By expedited review (days)	250	242	266	207	245	221
By orphans (days)	447	243	267	290*	332	354
By anticancer and immuno-modulators (days)	459	242	276	283	314	356

** Health Canada does not have an orphan policy; however, 20 NASs that were classified as orphan by either FDA, EMA or TGA were approved by Health Canada in 2021, with a median approval time of 290 days.*

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Approval at EMA 2021

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EMA **APPROVED A TOTAL OF 45 NASs IN 2021,** WITH A MEDIAN APPROVAL TIME OF **428 DAYS (TIME TO END OF SCIENTIFIC ASSESSMENT: 369 DAYS)**

THE MEDIAN EU COMMISSION TIME WAS 57 DAYS, THE AGENCY TIME 244 DAYS AND COMPANY TIME 133 DAYS

Type of Medicine

17 BIOLOGIC NASs APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **399 DAYS**

28 CHEMICAL NASs APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **451 DAYS**

21 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **459 DAYS**

24 NASs IN OTHER THERAPY AREAS APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **416 DAYS**

Designation and Review Type

4 EXPEDITED NAS APPROVALS IN 2021, WITH A MEDIAN APPROVAL TIME OF **250 DAYS;** THIS IS **184 DAYS FASTER** THAN THE MEDIAN OF THE **41 STANDARD NAS APPROVALS IN 2021**

16 ORPHAN NAS APPROVALS IN 2021, WITH A MEDIAN APPROVAL TIME OF **447 DAYS;** THIS IS **30 DAYS SLOWER** THAN THE MEDIAN OF THE **29 NON-ORPHAN NAS APPROVALS IN 2021**

Availability by EMA

22% OF THE NASs APPROVED IN 2021 BY EMA WERE APPROVED BY EMA **FIRST OR WITHIN ONE MONTH OF THEIR FIRST APPROVAL BY FDA, PMDA, HEALTH CANADA , SWISSMEDIC OR TGA**

78% OF THE NASs APPROVED IN 2021 BY EMA WERE APPROVED BY FDA, PMDA, HEALTH CANADA, SWISSMEDIC OR TGA **FIRST OR MORE THAN ONE MONTH BEFORE BEING APPROVED BY EMA**

THE MEDIAN **SUBMISSION GAP** TO EMA FOR THESE NASs WAS **97 DAYS**

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.

Approval at FDA 2021

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FDA (CDER AND CBER) **APPROVED A TOTAL OF 52 NASs IN 2021,** WITH A MEDIAN APPROVAL TIME OF **245 DAYS**

FOR THE NASs APPROVED 87% WERE 1-CYCLE REVIEWS, 13% 2-CYCLE REVIEWS

Type of Medicine

17 BIOLOGIC NASs APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **335 DAYS**

35 CHEMICAL NASs APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **244 DAYS**

24 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **242 DAYS**

28 NASs IN OTHER THERAPY AREAS APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **284 DAYS**

Designation and Review Type

37 EXPEDITED NAS APPROVALS IN 2021, WITH A MEDIAN APPROVAL TIME OF **242 DAYS;** THIS IS **123 DAYS FASTER** THAN THE MEDIAN OF THE **15 STANDARD NAS APPROVALS IN 2021**

28 ORPHAN NAS APPROVALS IN 2021, WITH A MEDIAN APPROVAL TIME OF **243 DAYS;** THIS IS **97 DAYS FASTER** THAN THE MEDIAN OF THE **24 NON-ORPHAN NAS APPROVALS IN 2021**

Availability by FDA

85% OF THE NASs APPROVED IN 2021 BY FDA WERE APPROVED BY FDA **FIRST OR WITHIN ONE MONTH OF THEIR FIRST APPROVAL BY EMA, PMDA, HEALTH CANADA , SWISSMEDIC OR TGA**

15% OF THE NASs APPROVED IN 2021 BY FDA WERE APPROVED BY EMA, PMDA, HEALTH CANADA, SWISSMEDIC OR TGA **FIRST OR MORE THAN ONE MONTH BEFORE BEING APPROVED BY FDA**

THE MEDIAN **SUBMISSION GAP** TO FDA FOR THESE NASs WAS **55 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.

Approval at PMDA 2021

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PMDA **APPROVED A TOTAL OF 38 NASs IN 2021,** WITH A MEDIAN APPROVAL TIME OF **301 DAYS (TIME TO END OF SCIENTIFIC ASSESSMENT: 272 DAYS)**

Type of Medicine

16 BIOLOGIC NASs APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **276 DAYS**

22 CHEMICAL NASs APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **329 DAYS**

14 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **276 DAYS**

24 NASs IN OTHER THERAPY AREAS APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **329 DAYS**

Designation and Review Type

17 EXPEDITED NAS APPROVALS IN 2021, WITH A MEDIAN APPROVAL TIME OF **266 DAYS;** THIS IS **65 DAYS FASTER** THAN THE MEDIAN OF THE **21 STANDARD NAS APPROVALS IN 2021**

16 ORPHAN NAS APPROVALS IN 2021, WITH A MEDIAN APPROVAL TIME OF **267 DAYS;** THIS IS **64 DAYS FASTER** THAN THE MEDIAN OF THE **22 NON-ORPHAN NAS APPROVALS IN 2021**

Availability by PMDA

26% OF THE NASs APPROVED IN 2021 BY PMDA WERE APPROVED BY PMDA **FIRST OR WITHIN ONE MONTH OF THEIR FIRST APPROVAL BY EMA, FDA, HEALTH CANADA , SWISSMEDIC OR TGA**

74% OF THE NASs APPROVED IN 2021 BY PMDA WERE APPROVED BY EMA, FDA, HEALTH CANADA, SWISSMEDIC OR TGA **FIRST OR MORE THAN ONE MONTH BEFORE BEING APPROVED BY PMDA**

THE MEDIAN **SUBMISSION GAP** TO PMDA FOR THESE NASs WAS **596 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.

Approval at Health Canada 2021

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HEALTH CANADA **APPROVED A TOTAL OF 34 NASs IN 2021,** WITH A MEDIAN APPROVAL TIME OF **301 DAYS (TIME TO END OF SCIENTIFIC ASSESSMENT: 300 DAYS)**

Type of Medicine

13 BIOLOGIC NASs APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **272 DAYS**

21 CHEMICAL NASs APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **301 DAYS**

20 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **283 DAYS**

14 NASs IN OTHER THERAPY AREAS APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **343 DAYS**

Designation and Review Type

9 EXPEDITED NAS APPROVALS IN 2021 WITH A MEDIAN APPROVAL TIME OF **207 DAYS;** THIS IS **136 DAYS FASTER** THAN THE MEDIAN OF THE **25 STANDARD NAS APPROVALS IN 2021**

HEALTH CANADA DOES NOT HAVE AN ORPHAN POLICY; HOWEVER, **20 NASs THAT WERE CLASSIFIED AS ORPHAN BY EITHER FDA, EMA OR TGA WERE APPROVED BY HEALTH CANADA IN 2021,** WITH A MEDIAN APPROVAL TIME OF **290 DAYS**

Availability by Health Canada

6% OF THE NASs APPROVED IN 2021 BY HEALTH CANADA WERE APPROVED BY HEALTH CANADA **FIRST OR WITHIN ONE MONTH OF THEIR FIRST APPROVAL BY EMA, FDA, PMDA, SWISSMEDIC OR TGA**

94% OF THE NASs APPROVED IN 2021 BY HEALTH CANADA WERE APPROVED BY EMA, FDA, PMDA, SWISSMEDIC OR TGA **FIRST OR MORE THAN ONE MONTH BEFORE BEING APPROVED BY HEALTH CANADA**

THE MEDIAN **SUBMISSION GAP** TO HEALTH CANADA FOR THESE NASs WAS **347 DAYS**

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

Approval at Swissmedic 2021

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SWISSMEDIC **APPROVED A TOTAL OF 37 NASs IN 2021** ,WITH A MEDIAN APPROVAL TIME OF **392 DAYS (TIME TO SCIENTIFIC ASSESSMENT: 303 DAYS)**

Type of Medicine

11 BIOLOGIC NASs APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **374 DAYS**

26 CHEMICAL NASs APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **410 DAYS**

19 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **314 DAYS**

18 NASs IN OTHER THERAPY AREAS APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **460 DAYS**

Designation and Review Type

3 EXPEDITED NAS APPROVALS IN 2021, WITH A MEDIAN APPROVAL TIME OF **245 DAYS;** THIS IS **154 DAYS FASTER** THAN THE MEDIAN OF THE **34 STANDARD NAS APPROVALS IN 2021**

18 ORPHAN NAS APPROVALS IN 2021, WITH A MEDIAN APPROVAL TIME OF **332 DAYS;** THIS IS **109 DAYS FASTER** THAN THE MEDIAN OF THE **19 NON-ORPHAN NAS APPROVALS IN 2021**

Availability by Swissmedic

3% OF THE NASs APPROVED IN 2021 BY SWISSMEDIC WERE APPROVED BY SWISSMEDIC **FIRST OR WITHIN ONE MONTH OF THEIR FIRST APPROVAL BY FDA, EMA, PMDA, HEALTH CANADA OR TGA**

97% OF THE NASs APPROVED IN 2021 BY SWISSMEDIC WERE APPROVED BY FDA, EMA, PMDA, HEALTH CANADA OR TGA **FIRST OR MORE THAN ONE MONTH BEFORE BEING APPROVED BY SWISSMEDIC**

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

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

Approval at TGA 2021

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TGA **APPROVED A TOTAL OF 35 NASs IN 2021**, WITH A MEDIAN APPROVAL TIME OF **350 DAYS**

Type of Medicine

14 BIOLOGIC NASs APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **330 DAYS**

21 CHEMICAL NASs APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **356 DAYS**

9 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **356 DAYS**

26 NASs IN OTHER THERAPY AREAS APPROVED IN 2021, WITH A MEDIAN APPROVAL TIME OF **350 DAYS**

Designation and Review Type

5 EXPEDITED NAS APPROVALS IN 2021 WITH A MEDIAN APPROVAL TIME OF **221 DAYS;** THIS IS **133 DAYS FASTER** THAN THE MEDIAN OF THE **30 STANDARD NAS APPROVALS IN 2021**

14 ORPHAN NAS APPROVALS IN 2021, WITH A MEDIAN APPROVAL TIME OF **354 DAYS;** THIS IS **11 DAYS SLOWER** THAN THE MEDIAN OF THE **21 NON-ORPHAN NAS APPROVALS IN 2021**

Availability in TGA

14% OF THE NASs APPROVED IN 2021 BY TGA WERE APPROVED BY TGA **FIRST OR WITHIN ONE MONTH OF THEIR FIRST APPROVAL BY FDA, EMA, PMDA, HEALTH CANADA OR SWISSMEDIC**

86% OF THE NASs APPROVED IN 2021 BY TGA WERE APPROVED BY FDA, EMA, PMDA, HEALTH CANADA OR SWISSMEDIC **FIRST OR MORE THAN ONE MONTH BEFORE BEING APPROVED BY TGA**

THE MEDIAN **SUBMISSION GAP** TO TGA FOR THESE NASs WAS **413 DAYS**

'Expedited review' refers to TGA 'Priority Review' 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

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Definitions: Facilitated regulatory pathways

	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
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 Worksharing	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	

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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.

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

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

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.

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)

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

Submission gap time
Time calculated from date of submission at the first regulatory agency to the date of regulatory submission to 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.

Continued: see next page

*The full list of NASs approved by each jurisdiction in 2021 will be available on the CIRS website.

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- 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.

Roll out time

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

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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, HTA and other healthcare stakeholders to meet, debate and develop regulatory and reimbursement policy through the innovative application of regulatory science and to facilitate access to pharmaceutical products. 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, special projects and grants.

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