Major improvements in the regulatory environment as well as changes in strategies of multinational companies have led to a general decrease in the time to marketing authorisation and improved consistency as well as an increase in the number of medicines that have become available over the last decade, 2009-2018, across six major regulatory agencies, namely 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). More specifically, the number of common products approved by all six agencies increased from 16 in 2009-2013 to 52 in 2014-2018.

Underlying factors influencing the overall time it takes for a new medicine to be submitted and then approved by an agency include company strategy, the conduct and the type of the review process, the type of the product and its therapeutic area; these aspects are analysed and discussed in this study. More specifically, facilitated regulatory pathways (FRPs) and orphan drug designation are major elements of the submission and approval strategies and are explored throughout this document. Nevertheless, one of the key factors that may determine the likelihood and timing of submission to subsequent markets is the size of the sponsor, which will be another point of focus for this Briefing.

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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 2018, FDA (CDER and CBER) approved the highest number of NASs (60), followed by EMA (40), Health Canada (34), PMDA (32), Swissmedic (31) and TGA (29) (Fig. 1). Despite these numbers varying on an annual basis, the overall number of NASs approved by the six agencies has increased for the past decade but subsequently flattened in 2018, except for FDA where there was still an increase, as shown by the three-year moving average. In addition, 2018 saw the highest total number of NASs approved for the past decade across each of the six agencies. A comparison of the numbers during the two parts of the decade, 2009-2013 and 2014-2018, revealed that the biggest difference in the number of approvals was seen for FDA, with a 54% increase, followed by EMA (48%), TGA (45%), Swissmedic (43%), PMDA (27%) and Health Canada (22%). The year-on-year variance across countries 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.

In 2018, FDA was the agency with the shortest median approval time (244 days), which is likely due to the wide use of facilitated regulatory pathways (FRPs) that year, where 25% of NAS approvals were designated as Breakthrough and 42% as Fast Track, highlighting the importance of those products in addressing unmet medical need. The fastest median approval time for FDA was followed by PMDA (323 days), Health Canada (348 days), TGA (363 days), EMA (436 days) and Swissmedic (519 days). In general, the median approval times were similar across the six agencies, where the difference between the fastest and slowest agency (excluding FDA) was 197 days, which is in line with the convergence in median times observed in the past (R&D Briefing 65 and 67). 2018 also saw a low variation in approval time (25th-75th percentile) (Fig. 2) for TGA (62 days) and PMDA (85 days), while EMA had the highest variation (180 days), which may be due to companies’ time (see Figure 13, p.9). Swissmedic remains the agency with the longest approval time, having increased by 49 days since 2018. The agency has been making changes to its review process, particularly the labelling phase, and more time may be needed to demonstrate the effect of those changes.
All six agencies now offer an expedited system (refers to EMA ‘Accelerated Assessment’, Swissmedic ‘Fast Track’ and FDA/PMDA/Health Canada/TGA ‘Priority Review’) designed to hasten the review process of promising NASs. TGA implemented its priority system in 2017 and three expedited approvals were granted in 2018. In 2018, the ratio of expedited approvals to standard reviews was highest for FDA (73%), followed by Health Canada (35%), PMDA (28%) Swissmedic (13%), EMA and TGA (10%). The proportion of expedited approvals has been consistently high for FDA and increasing when comparing 2009-2013 (results not shown) to 2014-2018 – 42% NASs were designated as expedited by FDA in first part of the decade compared with 63% in the second part. Although EMA experienced the most notable increase, from 7% in 2009-2013 to 15% in 2014-2018, the number of expedited approvals still remains the lowest, which is partially due to the fact the review type can be reverted back to standard if timelines cannot be met. In 2018, 3 NASs initially designated by EMA as expedited were reverted back to a standard review. Other agencies that also experienced an increase in expedited percentage when comparing 2009-2013 and 2014-2018 were Swissmedic (10% to 21%), PMDA (25% to 43%) and Health Canada (21% to 23%). Nevertheless, over the last five years, the proportion of expedited approvals by PMDA has decreased year-on-year.
The number of NASs with an orphan designation has increased across EMA, FDA, PMDA, Swissmedic and TGA, from 25% in 2009-2013 (results not shown) to 38% in 2014-2018. In 2009-2013 (Fig. 5), the proportion of orphans had a year-on-year variance but was generally high, which is most likely due to a combination of companies’ growing R&D pipelines, with an increased commitment from the agencies to tackle unmet medical needs. In 2018, FDA had the highest approval number for orphans (35 out of 60) while PMDA had the lowest (8 out of 32). Health Canada does not currently have an orphan policy; however, this agency approved 15 NASs in 2018 that were classified as orphan by either FDA, EMA or TGA.

Approval timelines were compared for orphans vs. non-orphans for 2014-2018 across the agencies (Fig. 6). All of the orphan NASs approved in Japan for the past five years have been through expedited review as an incentive from PMDA to fill the gap of unmet needs, and their median approval time in 2018 was 263 days. FDA had the fastest median approval time for orphans in 2018 (243 days) as 88% of these products have been approved through expedited review. Health Canada does not currently have an orphan policy; however, for the 15 NASs approved by Health Canada in 2018 that were classified as orphan by either FDA, EMA or TGA, the median approval time was 222 days, which is the fastest of all 6 agencies. Among the six agencies, EMA was the only one with median approval time longer for orphans than for non-orphans and this time has been increasing since 2016. Swissmedic median approval time for orphans has been increasing since 2015 and was similar to non-orphans in 2018. At TGA in 2018, 20% of orphan drugs were approved with the newly introduced priority review and their median approval time was slightly faster than that for non-orphans.
### New active substance (NAS) approval type

<table>
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<tr>
<th>Agency</th>
<th>Overall approvals</th>
<th>2018 NAS approvals, number</th>
<th>2018 NASs, % of 2018 approvals</th>
<th>Expedited, 2018 median approval time, days</th>
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**Characteristics: facilitated regulatory pathways**

**Figure 7: Facilitated regulatory pathway (FRP) and orphan status timelines across six agencies; focus on 2018**

Out of the six agencies, FDA offered (or made available) the greatest number of facilitated regulatory pathways (FRPs) to enable the availability, review and/or approval of medicines where there is an unmet medical need (Fig. 7 and 8). In 2018, 75% of NASs approved by FDA benefitted from at least one of the available FRPs. At the other agencies, FRPs ranged from 10% for TGA, where the agency introduced Priority Review in 2017, to 41% for Health Canada. Compounds reviewed through PMDA Sakigake had the quickest median approval time in 2018 (152 days), followed closely by TGA Priority Review (153 days). In EU, the PRIME programme launched in 2016 had 2 approvals; both were initially designated as Expedited but reverted to a standard approval due to legislated timelines for the sponsor to respond to questions.

**Figure 8: Proportion of NASs approved by each agency in 2018 that benefitted from at least one FRP (orphan excluded)**

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**EMA**

- Overall approvals: 40
- Expedited approvals: 4
- Median approval time: 249 days

**FDA**

- Overall approvals: 60
- Expedited approvals: 73
- Median approval time: 242 days

**PMDA**

- Overall approvals: 32
- Expedited approvals: 28
- Median approval time: 259 days

**Health Canada**

- Overall approvals: 34
- Expedited approvals: 35
- Median approval time: 209 days

**Swissmedic**

- Overall approvals: 31
- Expedited approvals: 13
- Median approval time: 267 days

**TGA**

- Overall approvals: 29
- Expedited approvals: 10
- Median approval time: 153 days

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TGA introduced an expedited (priority) review and provisional approval programme in 2017, with first decisions in 2018/2019. Health Canada does not currently have an orphan policy. 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 2014-2018, anti-infective therapies were approved marginally faster across all six agencies, with an overall median of 313 days, compared with 347 days for anti-cancer and immunomodulators, 353 days for cardiovascular, 372 days for alimentary and metabolism and 403 days for nervous system NASs. PMDA and FDA had the fastest approval times across the five therapy areas (Fig. 9). Nevertheless, as noted by the 25th-75th percentile bars, there were also wide variations for certain jurisdictions across therapy areas. This may reflect the more frequent use of expedited review pathways by agencies for specific therapy areas (Fig. 10).

Figure 9: NAS median approval time by therapeutic area (TA) for six regulatory authorities in 2014-2018, ordered by fastest agency median approval time within each TA

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.

Figure 10: NAS overall median approval time by therapeutic area in relation to expedited approvals for six regulatory authorities in 2014-2018

Therapy 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 to 2018 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.
A true comparison of regulatory performance can be derived from studying the review of compounds that were approved by all six agencies. This comparison was carried out for two time cohorts in the last ten years, namely 2009-2013 and 2014-2018, to determine whether any trends could be identified. Interestingly, the number of products approved by all six agencies in a five-year period increased from 16 NASs in 2009-2013 to 52 NASs in 2014-2018, which indicates that more products were becoming internationalised within this time frame. The overall length of time to registration, consisting of the submission gap and approval time (Fig. 11) may be a result of potential factors that impact registration of NASs. This may include company strategy to submit or target approval times at a particular agency, which is in turn influenced by the type of NASs as well as the use of expedited pathways within agencies to address unmet medical need for promising medicines. The briefing, as in the past (R&D Briefing 65 and 67) shows three waves of submission: first to EMA and FDA, then to Health Canada, Swissmedic and TGA, and finally to PMDA. The quickest time to registration was indeed at FDA for both cohorts, as a result of companies submitting there first as well as quick regulatory review times by the agency. Submissions to EMA occurred almost simultaneously with FDA, and the overall time to registration decreased, which may reflect the increased use of expedited pathways for products addressing unmet medical need by EMA. For the other four agencies, the submission gap generally increased between the two time frames, 2009-2013 and 2014-2018, although approval times decreased: this may be the result of companies’ strategies for better quality submissions to ensure approval. Although the longest submission gap occurred to PMDA, timing remained stable over the two time frames. PMDA has, however, pursued an effort to speed up the review of medicines, resulting in reduced approval time over the two time frames. Although the submission gap to Swissmedic more than doubled between the two time frames, the overall length of time to registration decreased due to reduced approval times.
Common approvals: orphan designation in the six agencies

The 52 NASs approved by all six authorities in 2014-2018 were subsequently analysed according to orphan designation status as well as company size (Fig. 12). Out of the 52 NASs, only 10 NASs received an orphan designation across all the authorities, which may be due to differences in criteria for obtaining the designation within each agency, as well as the differences in the indication submitted by the sponsor and eventually approved. Within each agency, for EMA, 17 of the NASs were designated as orphan, compared to 28 for FDA, 21 for PMDA, 22 for Swissmedic and 20 for TGA. Health Canada does not have an orphan policy, however this analysis considers NASs that were classified as orphan by either FDA, EMA or TGA and approved by Health Canada, with 29 NASs meeting such criteria. In general, the median submission gap for orphan NAS was longer compared to non-orphan NASs across all the authorities, which may be due to sponsor size. Indeed, the majority of orphan NASs were approved by non-top companies, highlighting the important role of smaller companies to drive innovation. On the other hand, the median approval timelines across all the agencies for orphan products were faster compared to non-orphans, which is likely due to the use of expedited pathways to prioritise the approval of such medicines.

Figure 12: Median submission gap and median approval time for NASs approved by all six authorities in 2014-2018 (52), based on orphan status and company size

Out of the 52 NASs approved by all six authorities during 2014-2018:

- 17 were designated as orphan by EMA
- 28 were designated as orphan by FDA
- 21 were designated as orphan by PMDA
- 22 were designated as orphan by Swissmedic
- 20 were designated as orphan by TGA

<table>
<thead>
<tr>
<th>Agency</th>
<th>Orphan (designated by)</th>
<th>Non-orphan (designated by)</th>
<th>Median time (days)</th>
<th>% - Proportion of non-top company approvals</th>
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<td>17</td>
<td>370, 388</td>
<td>65%, 17%</td>
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<tr>
<td>FDA</td>
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<td>214, 363</td>
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<td>PMDA</td>
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<td>356, 288</td>
<td>267, 315</td>
<td>62%, 29%</td>
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<tr>
<td>Health Canada</td>
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<td>166, 91</td>
<td>326, 355</td>
<td>43%, 18%</td>
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<tr>
<td>Swizzmedic</td>
<td>22</td>
<td>175, 96</td>
<td>421, 462</td>
<td>55%, 17%</td>
</tr>
<tr>
<td>TGA</td>
<td>20</td>
<td>226, 122</td>
<td>350, 372</td>
<td>60%, 16%</td>
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</table>

Health Canada does not currently have an orphan policy and this number shows the number of medicines that were approved by Health Canada that were classified as orphan by either FDA, EMA or TGA. Non top company is defined as having R&D budget<3 billion USD in 2017.
The decrease in the overall median approval time for EMA from 2014 to 2017 was driven largely by the decrease in company response time (Fig. 13): this time has increased in 2018, leading to an increase of the overall median time.

Furthermore, an important difference between expedited and standard NAS median approval times was the decrease in the EU Commission time for expedited NASs. The EMA time has remained rather stable since 2014. In 2017-2018, the EMA review time was approximately 1.5x faster for expedited review, owing to a shorter clock for Committee for Medicinal Products for Human Use (CHMP) opinion (150 days instead of 210 days). The expedited review was also characterised by an approximately four-times-faster company response time for both time periods (Fig. 14). However, the company response time has increased in 2017-2018 compared with the previous period. NASs approved via expedited review in 2017-2018 had an EU Commission time 21 days shorter than in 2014-2016 (35 vs. 56 days), compared with a 60-day review for standard products.

An analysis of NASs approved by either EMA, FDA or both revealed that 35 NASs approved by FDA in 2015-2017 had not been approved by EMA (due to lack of submission, review not finalised, sponsor withdrawal or rejection by the agency). 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. The gap is an absolute difference between the EMA and FDA time submission date.

"NAS only approved by EMA/FDA", may be due to: no submission, review not finalised, withdrawal by sponsor, rejection by the agency. 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. The gap is an absolute difference between the EMA and FDA time submission date.

The decrease in the overall median approval time for EMA from 2014 to 2017 was driven largely by the decrease in company response time (Fig. 13): this time has increased in 2018, leading to an increase of the overall median time. Furthermore, an important difference between expedited and standard NAS median approval times was the decrease in the EU Commission time for expedited NASs. The EMA time has remained rather stable since 2014. In 2017-2018, the EMA review time was approximately 1.5x faster for expedited review, owing to a shorter clock for Committee for Medicinal Products for Human Use (CHMP) opinion (150 days instead of 210 days). The expedited review was also characterised by an approximately four-times-faster company response time for both time periods (Fig. 14). However, the company response time has increased in 2017-2018 compared with the previous period. NASs approved via expedited review in 2017-2018 had an EU Commission time 21 days shorter than in 2014-2016 (35 vs. 56 days), compared with a 60-day review for standard products.

An analysis of NASs approved by either EMA, FDA or both revealed that 35 NASs approved by FDA in 2015-2017 had not been approved by EMA (due to lack of submission, review not finalised, sponsor withdrawal or rejection by the agency). 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. The gap is an absolute difference between the EMA and FDA time submission date.

‘NAS only approved by EMA/FDA’, may be due to: no submission, review not finalised, withdrawal by sponsor, rejection by the agency. 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. The gap is an absolute difference between the EMA and FDA time submission date.
The proportion of the FDA Center for Drug Evaluation and Research (CDER) NASs approved after one cycle increased between 2009-2013 and 2014-2018 from 74% to 86% (Fig. 17). The proportion of one and two-cycle reviews was higher for expedited compared with standard reviews in 2014-2018 (Fig. 18). This reflects CDER efforts to further optimise its review process for important medicines. An improvement in the number of one-cycle reviews may suggest better quality of dossiers, which in turn has a positive impact on review efficiency but it is important to note that this analysis only includes approvals: inclusion of compounds that have not been approved may generate a different perspective.

In 2018, FDA approved 15 BTD NASs, 93% of which were reviewed as expedited (priority) and only 13% of which were submitted by top companies (Fig. 19). The BTD NASs could have had other FRPs in place (Priority Review, Fast Track and Accelerated) and were generally from a range of therapy areas but were primarily anti-cancer and immunomodulator. Importantly, the BTD designation had an impact on the variance around approval time as well as the median development time (IND to submission).
PMDA approval numbers in fiscal year 2018 were generally similar to the other years (Fig. 20). PMDA generally approves medicines four times per fiscal year, between April and April, and consequently, analysis by calendar year may result in year-on-year fluctuations in the total numbers approved, compared with other agencies such as FDA, where the approvals can occur at any time of the year.

In 2018, the PMDA submission gap was 181 days, which was a large decrease from the 2016 spike of 763 days. This may be a result of companies’ changing strategies for submission to Japan as well as the decreasing impact of the legacy product gap (Fig. 21). Indeed the availability of older products to Japanese patients was facilitated in recent years through government programmes as well as through issues in the local development rights amongst sponsors (domestic versus foreign).

NASs approved by PMDA 2014-2018 were analysed according to submission gap length, where 25% products were unique to PMDA (no gap; only approved by PMDA; Fig. 22), where 50% of those were developed by Japanese companies (Fig. 23). A large proportion of medicines had a submission gap of less than a year (40%) which is larger than in 2017 (29%). Interestingly, these were not primarily high-need products; that is, expedited, nor were they orphan, or from major pharmaceutical companies, but again, a large proportion were from Japanese companies. Nevertheless, 35% of NASs had a submission gap of more than 1 year, many of these products were anti-cancer, orphans and expedited products, where in particular smaller companies (non-top), as well as multinational companies that go to a local Japanese sponsor to develop their product, may delay their submission to PMDA for strategic reasons.
The median submission gap to Health Canada decreased in 2018 to 325 days compared with 409 days in 2017. Conversely, the median approval time stayed very similar (Fig. 24). The overall submission gap and approval time 2016-2018 were also analysed according to review type (Fig. 25), where both the median approval time, as well as the submission gap were shorter for NASs designated as expedited (priority). This indicates that companies as well as the agency respectively fast-track the submission and approval of important products that address high unmet medical need.

The median submission gap to Health Canada decreased in 2018 for Health Canada, but the variance (25th-75th percentile) for the overall gap was slightly higher compared with 2016 and 2017. The submission gap to Health Canada varied according to the size of the sponsor, where either the median or the variance or both were larger in the case of non-top companies (Fig. 26). In 2018, the median submission gap from non-top companies was 918 days compared with 595 in 2017 and 157 in 2016, noting the large variance across all three years. Finally, the proportion of NASs from non-top companies was similar compared with 2017 (Fig. 27).
The median submission gap to Swissmedic increased in 2018 to 355 days, compared with 157 days in 2017, similarly to the median approval which increased from 470 (2017) to 519 days (2018) (Fig. 28). The overall submission gap and median approval time 2016-2018 were also analysed according to review type: they were both faster for NASs designated as expedited (Fast Track) or using the Procedure with Prior Notification (PPN), which offers a 20% faster review for a 100% surcharge in user fees (Fig. 29). The agency has introduced in 2016 a system where sponsors not granted expedited (Fast Track) can automatically switch to PPN to speed up the review.

The median submission gap to Swissmedic increased in 2018 to 355 days, compared with 157 days in 2017, similarly to the median approval which increased from 470 (2017) to 519 days (2018) (Fig. 28). The overall submission gap and median approval time 2016-2018 were also analysed according to review type: they were both faster for NASs designated as expedited (Fast Track) or using the Procedure with Prior Notification (PPN), which offers a 20% faster review for a 100% surcharge in user fees (Fig. 29). The agency has introduced in 2016 a system where sponsors not granted expedited (Fast Track) can automatically switch to PPN to speed up the review.

The increase in the overall submission gap to Swissmedic may be as a result of more NASs being approved from non-top companies (Fig. 30). Similarly to Health Canada (p.12) and TGA (p.14), the submission gap from non-top sponsors was longer in terms of median and/or had larger variance compared with top companies (Fig. 31).
The median submission gap to TGA decreased in 2018 to the third of 2017 gap. Conversely, the median approval time stayed very similar (Fig. 32). Three NASs were approved by TGA in 2018 under the newly introduced Priority Review with an approval time of 153 days (Fig. 33). One of those NASs, which was in fact the fastest out of the three expedited approvals, was based on the Australia-Canada-Singapore-Switzerland (ACSS) Consortium’s New Chemical Entities Work Sharing Trial, where the pilot drug submission was jointly reviewed by TGA and Health Canada. Across all three expedited NASs, the submission gap to TGA was similar compared with standard (148 vs. 161 days).

Similarly to Health Canada and Swissmedic, the submission gap to TGA varied according to sponsor size, where NASs developed by non-top companies had longer median times and/or larger variance (Fig. 34 and 35). Overall, the submission gap to TGA has decreased in 2018 compared to previous year, and specifically both for top and non-top companies. Variance for non-top companies was also smaller for 2018, particularly compared to 2016.
EMA APPROVED A TOTAL OF 40 NASs IN 2018, WITH A MEDIAN APPROVAL TIME OF 436 DAYS

- 24 BIOLOGIC NASs APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 436 DAYS
- 16 CHEMICAL NASs APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 447 DAYS
- 26 NASs IN OTHER THERAPY AREAS APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 436 DAYS
- 14 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 465 DAYS
- 4 EXPEDITED NAS APPROVALS IN 2018, WITH A MEDIAN APPROVAL TIME OF 249 DAYS; THIS IS 206 DAYS FASTER THAN THE MEDIAN OF THE 36 STANDARD NAS APPROVALS IN 2018
- 17 ORPHAN NAS APPROVALS IN 2018, WITH A MEDIAN APPROVAL TIME OF 463 DAYS; THIS IS 34 DAYS SLOWER THAN THE MEDIAN OF THE 23 NON-ORPHAN NAS APPROVALS IN 2018

80% OF THE NASs APPROVED IN 2018 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 59 DAYS

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FDA (CDER AND CBER) APPROVED A TOTAL OF 60 NASs IN 2018, WITH A MEDIAN APPROVAL TIME OF 244 DAYS

19 BIOLOGIC NASs APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 308 DAYS

41 CHEMICAL NASs APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 243 DAYS

20 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 245 DAYS

40 NASs IN OTHER THERAPY AREAS APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 243 DAYS

44 EXPEDITED NAS APPROVALS IN 2018, WITH A MEDIAN APPROVAL TIME OF 242 DAYS; THIS IS 121 DAYS FASTER THAN THE MEDIAN OF THE 16 STANDARD NAS APPROVALS IN 2018

35 ORPHAN NAS APPROVALS IN 2018, WITH A MEDIAN APPROVAL TIME OF 243 DAYS; THIS IS 68 DAYS FASTER THAN THE MEDIAN OF THE 25 NON-ORPHAN NAS APPROVALS IN 2018

75% OF THE NASs APPROVED IN 2018 BY FDA WERE APPROVED BY FDA FIRST OR WITHIN ONE MONTH OF THEIR FIRST APPROVAL BY EMA, PMDA, HEALTH CANADA, SWISSMEDIC OR TGA

25% OF THE NASs APPROVED IN 2018 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 260 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 32 NASs in 2018, with a median approval time of 323 days.

- 14 Biologic NASs approved in 2018, with a median approval time of 332 days.
- 18 Chemical NASs approved in 2018, with a median approval time of 301 days.
- 11 Anti-cancer and immunomodulator NASs approved in 2018, with a median approval time of 306 days.
- 21 NASs in other therapy areas approved in 2018, with a median approval time of 332 days.
- 9 expedited NAS approvals in 2018, with a median approval time of 259 days; this is 77 days faster than the median of the 23 standard NAS approvals in 2018.
- 8 orphan NAS approvals in 2018, with a median approval time of 263 days; this is 71 days faster than the median of the 24 non-orphan NAS approvals in 2018.

31% of the NASs approved in 2018 by PMDA were approved by PMDA first or within one month of their first approval by EMA, FDA, Health Canada, Swissmedic or TGA.

69% of the NASs approved in 2018 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 654 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 2018, WITH A MEDIAN APPROVAL TIME OF 348 DAYS

11 BIOLOGIC NASs APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 338 DAYS

23 CHEMICAL NASs APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 349 DAYS

11 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 350 DAYS

23 NASs IN OTHER THERAPY AREAS APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 343 DAYS

12 EXPEDITED NASs APPROVED IN 2018 WITH A MEDIAN APPROVAL TIME OF 209 DAYS; THIS IS 141 DAYS FASTER THAN THE MEDIAN OF THE 22 STANDARD NAS APPROVALS IN 2018

HEALTH CANADA DOES NOT HAVE AN ORPHAN POLICY; HOWEVER, 15 NASs THAT WERE CLASSIFIED AS ORPHAN BY EITHER FDA, EMA OR TGA WERE APPROVED BY HEALTH CANADA IN 2018, WITH A MEDIAN APPROVAL TIME OF 222 DAYS

6% OF THE NASs APPROVED IN 2018 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 2018 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 361 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.
SWISSMEDIC APPROVED A TOTAL OF 31 NASs IN 2018, WITH A MEDIAN APPROVAL TIME OF 519 DAYS.

11 BIOLOGIC NASs APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 499 DAYS.

20 CHEMICAL NASs APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 527 DAYS.

8 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 460 DAYS.

23 NASs IN OTHER THERAPY AREAS APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 525 DAYS.

4 EXPEDITED NAS APPROVALS IN 2018, WITH A MEDIAN APPROVAL TIME OF 267 DAYS; THIS IS 262 DAYS FASTER THAN THE MEDIAN OF THE 27 STANDARD NAS APPROVALS IN 2018.


13% OF THE NASs APPROVED IN 2018 BY SWISSMEDIC WERE APPROVED BY SWISSMEDIC FIRST OR WITHIN ONE MONTH OF THEIR FIRST APPROVAL BY FDA, EMA, PMDA, HEALTH CANADA OR TGA.

87% OF THE NASs APPROVED IN 2018 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 525 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.
TGA APPROVED A TOTAL OF 29 NASs IN 2018, WITH A MEDIAN APPROVAL TIME OF 363 DAYS

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<thead>
<tr>
<th>Type of Medicine</th>
<th>Approval at TGA 2018</th>
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<tr>
<td>11 BIOLOGIC NASs</td>
<td>APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 363 DAYS</td>
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<tr>
<td>18 CHEMICAL NASs</td>
<td>APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 359 DAYS</td>
</tr>
<tr>
<td>13 ANTI-CANCER AND IMMUNOMODULATOR NASs</td>
<td>APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 365 DAYS</td>
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<tr>
<td>16 NASs IN OTHER THERAPY AREAS</td>
<td>APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 348 DAYS</td>
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<tr>
<td>3 EXPEDITED NASs</td>
<td>APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 153 DAYS; THIS IS 212 DAYS FASTER THAN THE MEDIAN OF THE 26 STANDARD NASs APPROVALS IN 2018</td>
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<tr>
<td>10 ORPHAN NASs</td>
<td>APPROVED IN 2018, WITH A MEDIAN APPROVAL TIME OF 335 DAYS; THIS IS 31 DAYS FASTER THAN THE MEDIAN OF THE 19 NON-ORPHAN NAS APPROVALS IN 2018</td>
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93% OF THE NASs APPROVED IN 2018 BY TGA WERE APPROVED BY FDA, EMA, PMDA, HEALTH CANADA OR SWISSMEDIC FIRST OR WITHIN ONE MONTH OF THEIR FIRST APPROVAL BY FDA, EMA, PMDA, HEALTH CANADA OR SWISSMEDIC

7% OF THE NASs APPROVED IN 2018 BY TGA WERE APPROVED BY TGA FIRST OR WITHIN ONE MONTH OF THEIR FIRST APPROVAL BY FDA, EMA, PMDA, HEALTH CANADA OR SWISSMEDIC. THE MEDIAN SUBMISSION GAP TO TGA FOR THESE NASs WAS 163 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.

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<td>TGA Provisional Approval</td>
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</table>
**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.

**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)

**Rollout time**  
Date of submission at the first regulatory agency to the date of regulatory approval at the target agency.

**Submission gap**  
Date of submission at the first regulatory agency to the date of regulatory submission to the target agency.

**Top company**  

**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.
- C - Cardiovascular: Cardiac therapy, antihypertensives, beta blocking agents, calcium channel blockers, agents acting on the renin-angiotensin system, serum lipid reducing agents.
- 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.

*The full list of NASs approved by each jurisdiction in 2018 will be made available on the CIRS website.*

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Acknowledgements

We are most grateful to Professor Mamoru Narukawa (Kitasato University Graduate School of Pharmaceutical Sciences, Japan), Health Canada, Canada, the Therapeutic Goods Administration, Australia, Swissmedic, Switzerland for validating the approval data for PMDA, Health Canada, TGA and Swissmedic respectively that we have used in order to generate the analysis.

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