# R&D BRIEFING 59

# The impact of the evolving regulatory environment on the approval of new medicines across six major authorities 2006-2015

The last decade, 2006-2015, has seen a continuation of the convergence and general decrease in the approval times amongst six major regulatory authorities, namely the European Medicines Agency (EMA), the US Food and Drug Authority (FDA), the Japanese Pharmaceuticals and Medical Devices Agency (PMDA), Health Canada, Swissmedic and the Australian Therapeutic Goods Administration (TGA).

Convergence in approval times has resulted in compounds being internationalised in a shorter time frame in the recent years. The second half of the decade, 2011-2015, also saw a major increase in the number of approvals of anti-cancer and immunomodulator new active substances (NASs), compared with 2006-2010, and these now constitute approximately a third of all NAS approvals across the six agencies.

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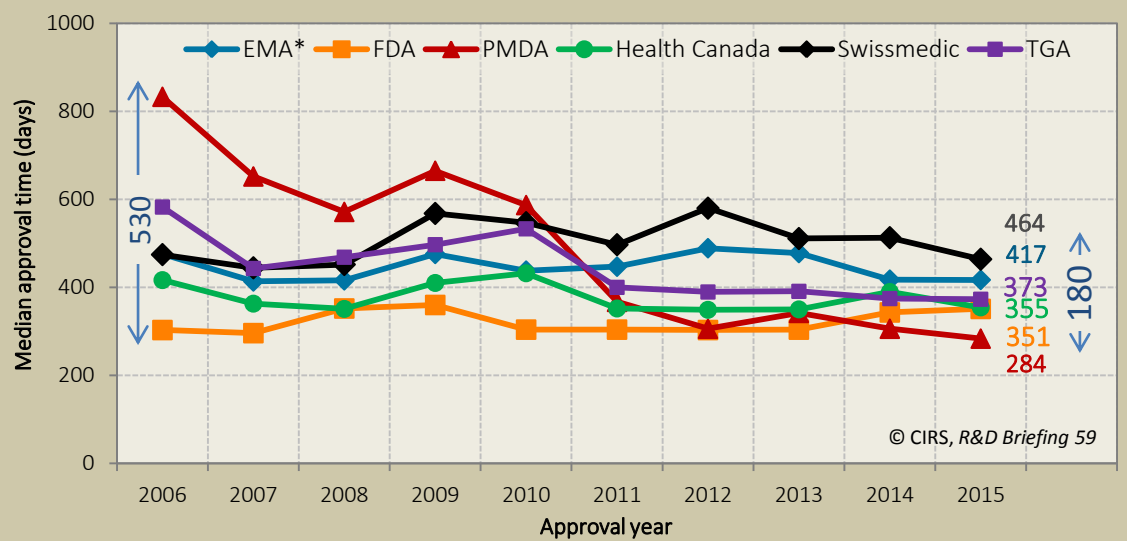
The six agencies have continued to put initiatives in place to improve the quality and timeliness of review, which may explain their general decrease and tightening in approval times. One area agencies have been concentrating on is improvement of the company submissions ahead of the agency assessment in order to ensure that target timelines are met. Such activities further improve consistency and predictability of the review, but have also impacted the overall approval time either in a positive or negative matter as seen in the last decade.

New active substance (NAS) median approval time for six regulatory authorities in 2006-2015




*The EMA approval time includes the EU Commission time.



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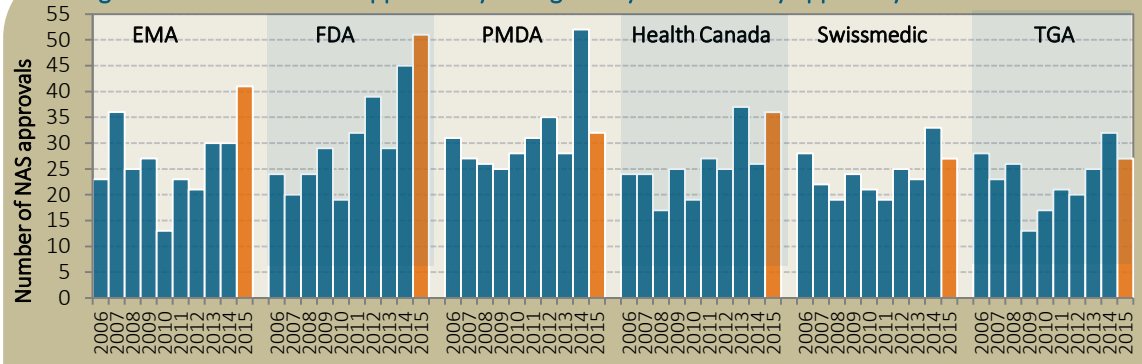
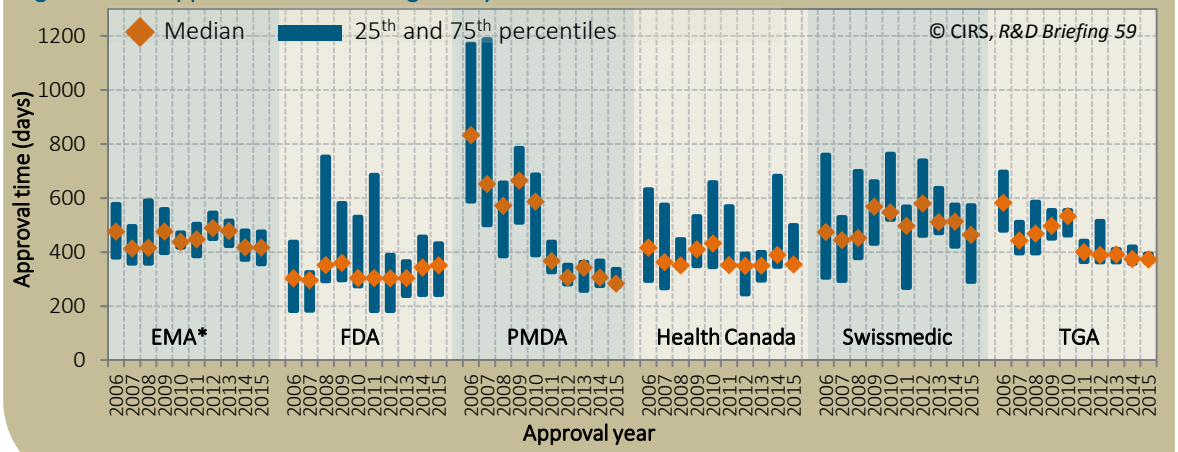
Figure 1: Number of NASs approved by six regulatory authorities by approval year 2006-2015




**In 2015, FDA approved the highest number of NASs (51), which was also the top number for FDA in the last decade. The FDA was followed in 2015 by EMA (41), Health Canada (36), PMDA (32), Swissmedic (27) and TGA (27) (Figure 1).** The overall number of NASs approved by the six agencies has increased when comparing 2006-2010 and 2011-2015. Looking at each agency, the biggest difference in the number of approvals when comparing the two parts of the decade was seen for FDA, with a 69% increase in NAS approvals, followed by Health Canada (39%), PMDA (30%), EMA (17%), TGA (17%) and Swissmedic (11%). A number of the NASs were ultimately approved by all or most of the six agencies, but certain factors, such as company size or strategy, resulted in the fact that not all NASs were internationalised. This in turn may explain the year-on-year variance across countries in the number of products approved by each agency, but it is important to note that the actual number of products approved is also influenced by the agency performance.

Figure 2: NAS approval time for six regulatory authorities in 2006-2015

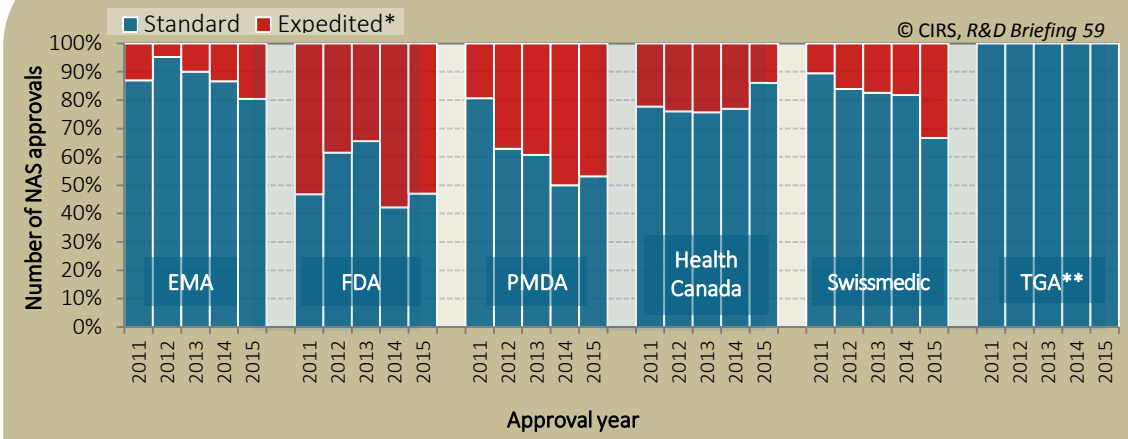



*The EMA approval time includes the EU Commission time.

**The convergence in median approval time observed in the previous years (*R&D Briefing 55* and *57*) continued in 2015, when the difference in the median approval time between the fastest and the slowest agency decreased from 530 days in 2006 to 180 days in 2015 (cover page Figure).** This may reflect the improving quality of submissions from companies, as well as implementation of various quality measures by agencies, such as pre-submission activities in order to verify the quality of the dossier ahead of the review (page 9). In 2015, PMDA was the agency with the shortest median approval time (284 days), followed by FDA (351), Health Canada (355), TGA (373), EMA (417) and Swissmedic (464). Interestingly, the gap between FDA and PMDA has further widened in 2015 to 67 days. Amongst the cohort of EMA, Health Canada, TGA and FDA the gap is similar at 66 days, but this gap has been narrowing. The large drop in the PMDA approval times that has occurred since the beginning of the decade reflects the continual improvements and resource commitments made by the agency. Although the FDA timing has increased since 2013, this is likely due to changes in the approval process under the fifth iteration of the Prescription Drug User Fee (PDUFA V) legislation (page 9). Besides a decrease in variability in approval times across the six agencies, the past years have also seen a decrease in variation in approval time (25th - 75th percentile) within the agencies, especially for TGA, EMA and PMDA, which have established even more consistency in review timing in the last five years (Figure 2).

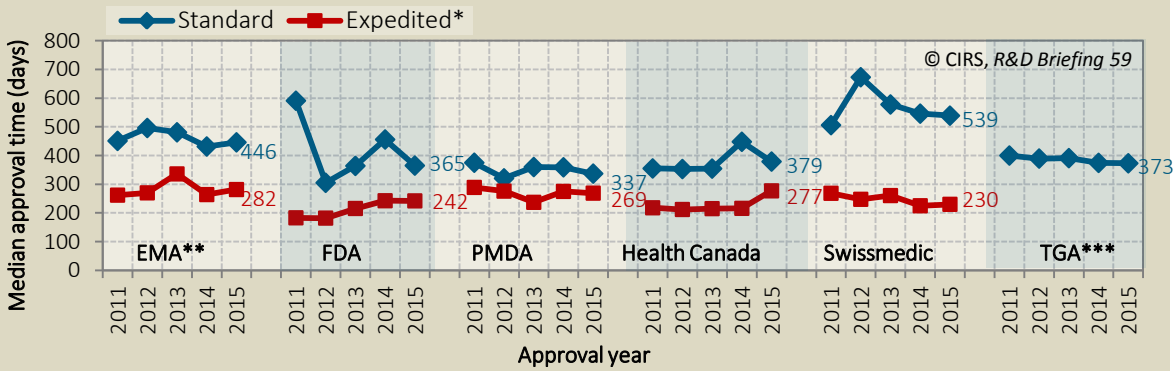
Figure 3: Number of NAS approvals by review type for six regulatory authorities in 2011-2015




*'Expedited review' refers to EMA 'Accelerated Assessment' and FDA/PMDA/Health Canada/Swissmedic 'Priority Review'.
**TGA does not currently have an expedited evaluation programme.

**Currently, EMA, FDA, PMDA Health Canada and Swissmedic offer an expedited priority system (refers to EMA 'Accelerated Assessment' and FDA/PMDA/Health Canada/Swissmedic 'Priority Review') designed to hasten the review process of promising NASs (Figure 3)** .The proportion of expedited approvals has been consistently high for FDA and PMDA in the last few years. The two agencies had the highest percentage of expedited approvals in 2015, at approximately 53% (FDA) and 47% (PMDA), compared with 33% for Swissmedic, 20% for EMA and 14% for Health Canada. TGA, following changes in the registration process in 2010, no longer has a formal expedited evaluation system. The proportion of applications that qualified for an expedited review increased for all five agencies in 2015 compared with 2011-2014. Swissmedic experienced the most notable increase (from 16% in 2011-2014 to 33% in 2015), followed by EMA (11% to 20%), PMDA (38% to 47%) and FDA (47% to 53%). More time is needed to see whether these changes reflect a long-term trend, particularly at EMA with the launch of the PRIME (PRIority MEdicines) scheme in 2016, which is specifically designed to promote the usage of accelerated assessment for medicines that aim to address unmet medical need.

Figure 4: NAS median approval time by review type for six regulatory authorities in 2011-2015




*'Expedited review' refers to EMA 'Accelerated Assessment' and FDA/PMDA/Health Canada/Swissmedic 'Priority Review'.
**The EMA approval time includes the EU Commission time.
***TGA does not currently have an expedited evaluation programme.

**For 2015, the overall median approval time across the six agencies for standard review was 407 days, compared with 265 days for expedited review.** In 2015, the agency with the greatest difference in median approval time between expedited and standard review was Swissmedic with a difference of 309 days (Fig. 4), whereas the smallest difference was for PMDA with 68 days; the gap for other agencies was 164 days for EMA, 102 days for Health Canada, and 123 days for FDA. The expedited approval time continued to climb at FDA, which has increased by 60 days since 2012, and this may be in part due to the additional two-month period introduced to the review timeline under PDUFA V.

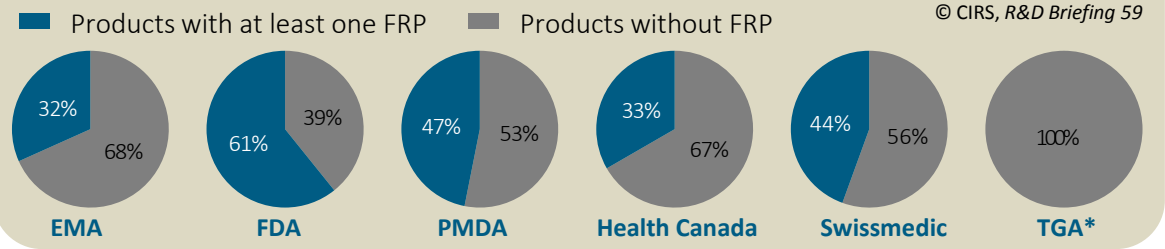
 

Figure 5: Facilitated regulatory pathway usage and timelines across six agencies; focus on 2015

| © CIRS, *R&D Briefing 59* | Facilitated regulatory pathway | 2015 approval, number | 2015 approval, percentage | 2015 median approval time, days |
|---|---|---|---|---|
| **EMA** *The EMA approval time includes the EU Commission time.* | **Overall approvals** | **41** | | **417** |
| | Accelerated (referred to in this Briefing as Expedited) | 8 | 20% | 282 |
| | Conditional | 3 | 7% | 428 |
| | Exceptional | 2 | 5% | 476 |
| | | | | |
| **FDA** | **Overall approvals** | **51** | | **351** |
| | Priority (referred to in this Briefing as Expedited) | 27 | 53% | 242 |
| | Accelerated (NOTE: all compounds in this case were also designated as Priority) | 6 | 12% | 168 |
| | Breakthrough (NOTE: all compounds in this case were also designated as Priority) | 10 | 20% | 207 |
| | Fast Track (NOTE: 13 of these compounds were also designated as Priority) | 17 | 33% | 304 |
| | | | | |
| **PMDA** | **Overall approvals** | **32** | | **284** |
| | Priority (referred to in this Briefing as Expedited) | 15 | 47% | 269 |
| | Sagikake | - | - | - |
| | | | | |
| **Health Canada** | **Overall approvals** | **36** | | **355** |
| | Priority (referred to in this Briefing as Expedited) | 5 | 14% | 277 |
| | Conditional (Notice of Compliance with conditions; NOC/c) | 7 | 19% | 327 |
| | | | | |
| **Swissmedic** | **Overall approvals** | **27** | | **464** |
| | Priority (referred to in this Briefing as Expedited) | 9 | 33% | 230 |
| | Procedure with prior notification (Verfahren mit Voranmeldung; VmVA) | 3 | 11% | 407 |
| | | | | |
| **TGA*** | **Overall approvals** | **27** | | **373** |
| | | | | |
| | | | | |

**Out of the six agencies, FDA used 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 (Figure 5).** In 2015, 61% of NASs approved by FDA benefitted from at least one of the available FRPs, compared with 47% at PMDA, 44% at Swissmedic, 33% at Health Canada, 32% at EMA (Figure 6). TGA does not currently offer any FRPs to expedite the availability, review and/or approval of medicines. Across the various FRPs for the five agencies using them, compounds which included FDA Accelerated Assessment had the fastest median approval time in 2015 (168 days), followed by the FDA Breakthrough Designation (207 days). Nevertheless, it should be noted that many compounds reviewed at FDA often take advantage of multiple FRPs, which generally results in a faster approval time (*R&D Briefing 57*).

Figure 6: Proportion of NASs approved by each agency in 2015 that benefitted from at least one FRP




*TGA does not currently have an expedited evaluation programme.

Figure 7: Percentage of NAS approvals by compound type for six regulatory authorities in 2006-2010 and 2011-2015

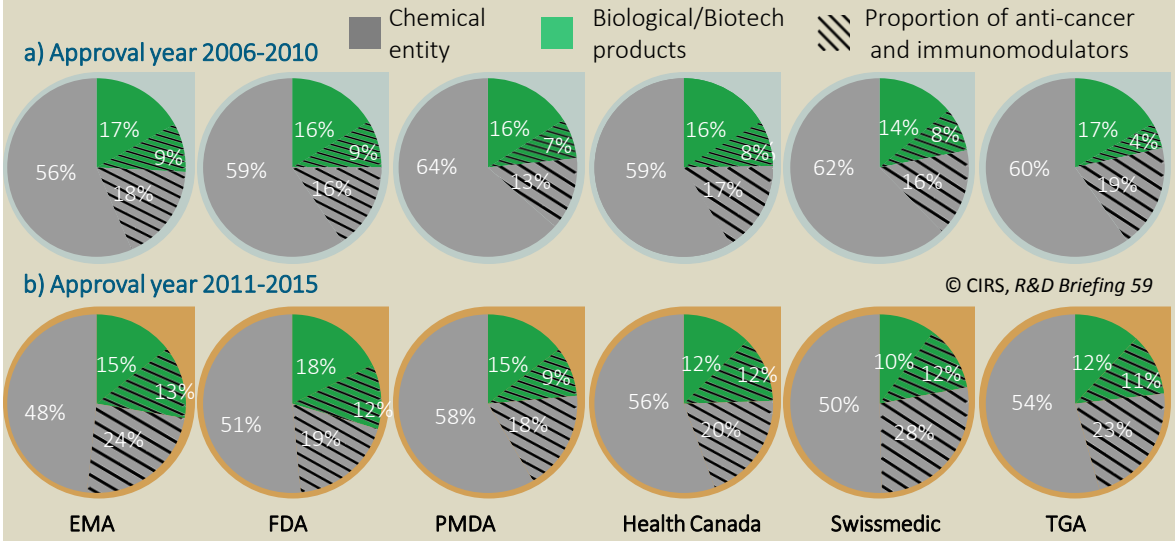
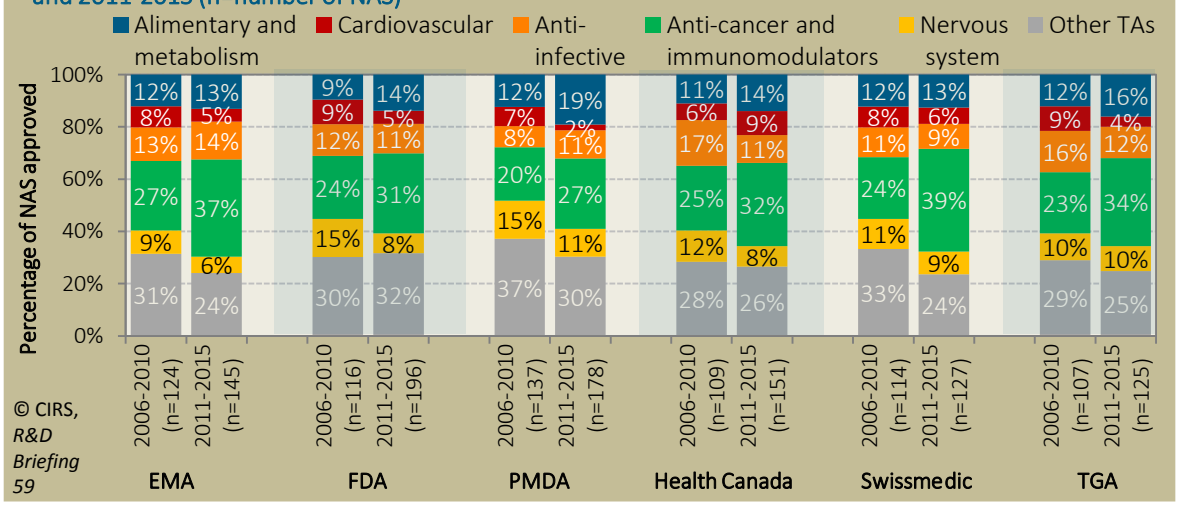



Figure 8: NAS median approval time (days) by compound type for six regulatory authorities in 2011- 2015 (all therapy areas)

| | Chemical entity | Biological/Biotech product |
|---|---|---|
| **EMA** | 450 | 441 |
| **FDA** | 306 | 334 |
| **PMDA** | 324 | 313 |
| **Health Canada** | 352 | 356 |
| **Swissmedic** | 497 | 518 |
| **TGA** | 391 | 371 |

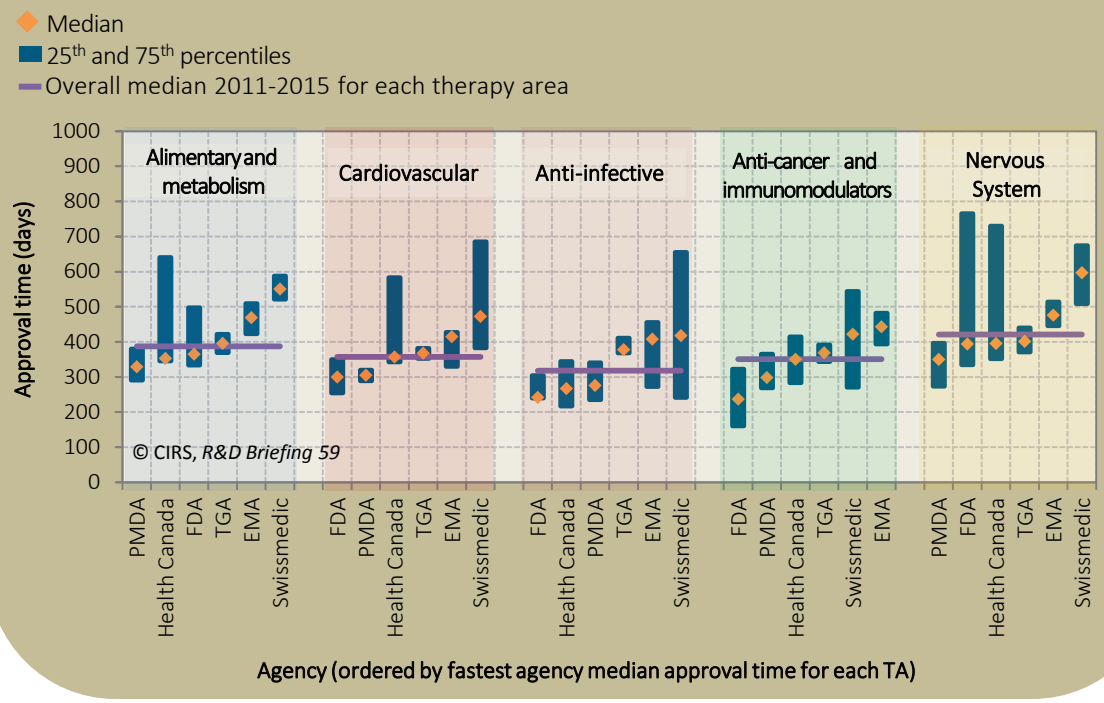
**The majority of anti-cancer and immunomodulator NASs approved both in 2006-2010 and 2011-2015 were small molecules (chemical entity).** Although the proportion of chemical entities and biological/biotech products remained similar when comparing the two parts of the decade, the proportion of anti-cancer and immunomodulator compounds increased for each agency, both in the biological/biotech and chemical entity areas. There was little difference in the median approval time between chemical entities and the biological/biotech products across the six agencies (Figure 8).

Figure 9: Percentage of NAS approvals by therapeutic area (TA) for six regulatory authorities in 2006-2010 and 2011-2015 (n=number of NAS)




**The second half of the decade, 2011-2015, saw a major increase in the approval of anti-cancer and immunomodulator NASs across the six agencies, compared with 2006-2010. As a result, in 2011-2015, approximately a third of all approvals by the six agencies were anti-cancer and immunomodulator NASs.** There was a moderate increase in alimentary and metabolism NASs and a general drop in the proportion of cardiovascular and nervous system NASs. There was also a proportional drop in the category of 'other therapy areas', which may be due to companies putting more emphasis on the development of compounds in the top therapy areas.

Figure 10: NAS approval time by therapeutic area (TA) for six regulatory authorities in 2011-2015, ordered by fastest agency median approval time within each TA




**In 2011-2015, PMDA, Health Canada and FDA had the fastest approvals across all five therapy areas (Figure 10), with median approval times at or below the overall median.** Nevertheless, as noted by the 25th - 75th percentile bars, there were also wide variations for certain jurisdictions across therapy areas; for example, Health Canada's approval timing for alimentary and metabolism, cardiovascular and nervous system NASs was highly variable compared with low timing variability for approval of anti-infective and anti-cancer and immunomodulators therapies. Overall, anti-infective therapies were approved faster than all other therapy areas, at 318 days, compared with 351 days for anti-cancer and immunomodulators, 357 days for cardiovascular, 387 days for alimentary and metabolism and 421 days for nervous system NASs. This may reflect the more frequent usage of expedited review pathways for certain therapy areas with short approval times (Figure 11). There were also variations within each therapy area for the six agencies and this is also likely due to the differences in usage of those pathways, which are generally used more frequently by FDA and PMDA.

Figure 11: NAS median approval time (days) by therapeutic area for six regulatory authorities in 2011-2015 (%)=proportion of expedited approvals*

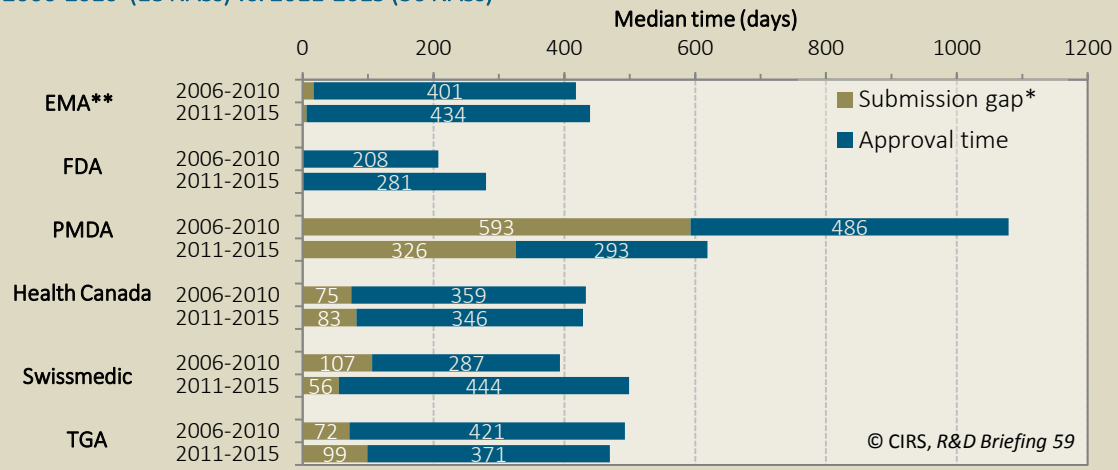
| © CIRS, *R&D Briefing 59* | Alimentary and metabolism | Cardiovascular | Anti-infective | Anti-cancer and immuno-modulators | Nervous system |
|---|---|---|---|---|---|
| EMA** | 469 (5%) | 415 (14%) | 408 (33%) | 443 (13%) | 476 (0%) |
| FDA | 365 (33%) | 300 (50%) | 242 (77%) | 237 (72%) | 394 (20%) |
| PMDA | 329 (24%) | 305 (25%) | 276 (74%) | 299 (71%) | 350 (26%) |
| Health Canada | 353 (24%) | 357 (14%) | 267 (50%) | 351 (25%) | 396 (0%) |
| Swissmedic | 551 (0%) | 473 (25%) | 418 (33%) | 422 (36%) | 597 (0%) |
| TGA*** | 396 (0%) | 368 (0%) | 378 (0%) | 369 (0%) | 402 (0%) |

*'Expedited review' refers to EMA 'Accelerated Assessment' and FDA/PMDA/Health Canada/Swissmedic 'Priority Review'.
**The EMA approval time includes the EU Commission time.
***TGA does not currently have an expedited evaluation programme.

**A true comparison of regulatory performance can be derived from studying the review of compounds that were approved by all compared agencies. It was possible to identify 18 NASs that were approved by the six agencies within 2006-2010 time frame, and 36 NASs that were approved in 2011-2015.** The submission gap and approval time for each agency for these compounds (Figure 12) as well as the overall rollout for both timescales (Figure 13) uncovered some of the limiting factors for the medicines to reach the market, which may include company strategy to submit later or long approval times at a particular agency. Unsurprisingly, the quickest rollout was to US for both 2006-2010 and 2011-2015. Although the rollout to Japan occurred last out of the six countries for both time periods, both submission gap and approval time have decreased from 2006-2010 to 2011-2015. This reflects both PMDA efforts to speed up the review of medicines as well as changes in companies' strategies, which now include earlier submissions to PMDA.. The most notable changes made by the agency include an increase in resources, the introduction of prior-evaluation meetings to discuss clinical trial study results, as well as the prior-assessment consultations approximately 6 months prior to submission of a new drug application. The general strategy for international products appears to be simultaneous submission to EMA and FDA, followed by Health Canada, Swissmedic and TGA and finally PMDA.

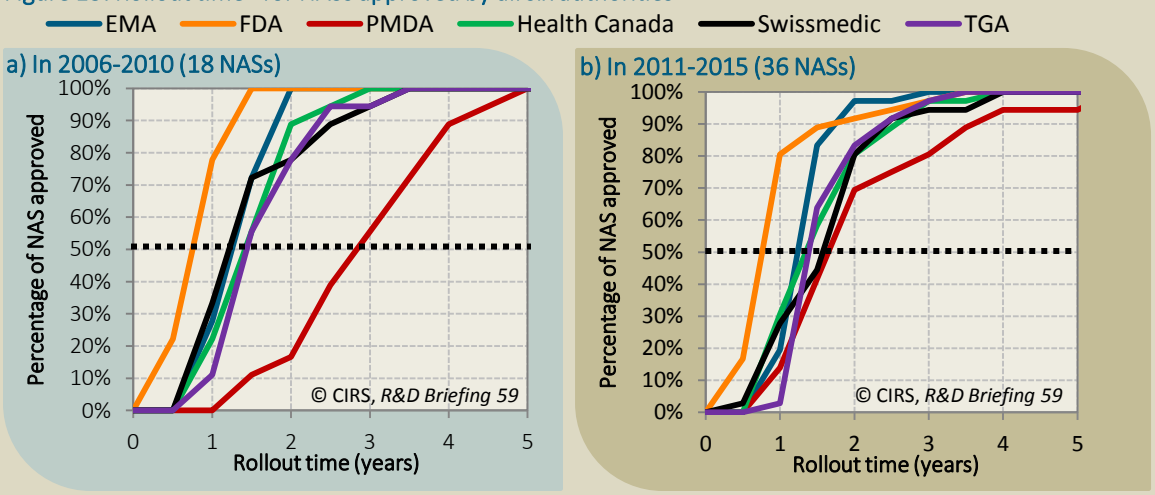
Figure 12: Median submission gap* and median approval time for NASs approved in all six authorities in 2006-2010 (18 NASs) vs. 2011-2015 (36 NASs)




*Date of submission at the first regulatory agency to the date of regulatory submission to the target agency.
**The EMA approval time includes the EU Commission time.

**The convergence in timings for the six agencies was reflected not only by approval time, but also by the overall rollout (Figure 13).** In 2006-2010, it took 3 years to approve 50% of the NASs (in this case, 9 NASs) by all agencies, whereas the time to approve half of the NASs (18) at all agencies was reduced to approximately 1.5 years in 2011-2015. This is largely due to the tightening of the PMDA timelines, as a result in the decrease of both the submission gap and approval time.

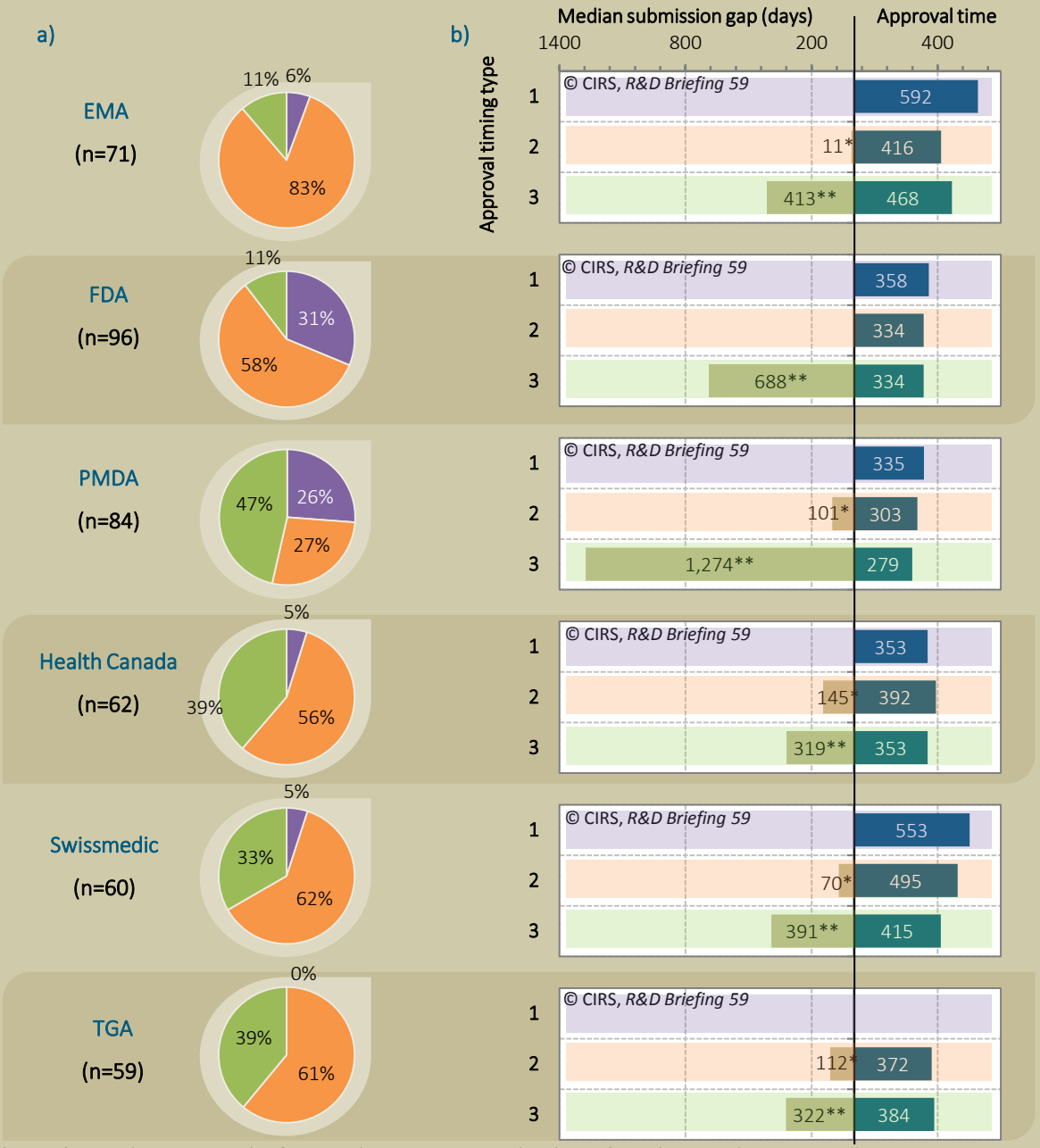
Figure 13: Rollout time* for NASs approved by all six authorities




*Date of submission at the first regulatory agency to the date of regulatory approval at the target agency.
**The EMA approval time includes the EU Commission time.

Figure 14: Effect of approval timing on the median submission time and median approval time for NASs approved in 2014-2015 by each of the six agencies a) Breakdown of NASs by approval type 1-3 (n=number of NASs) b) Median submission gap and approval time for each approval type 1-3

**Type 1:** No previous submission/approval (product approved only in the jurisdiction)
**Type 2:** Concurrent approval with another agency (submission to agency occurs prior to first-in-world approval)
**Type 3:** Follow-on approval (submission to agency occurs following first-in-world approval)




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

**The type of approval and its timing were also shown to affect the time to approval for NASs approved by the six agencies 2014-2015.** FDA and PMDA approved the largest number of NASs out of the six agencies that were only approved by each of the jurisdictions (type 1). EMA approved mostly products that were approved concurrently with another jurisdiction(s), where submission occurred prior to first-in-world approval (type 2). PMDA, Health Canada, Swissmedic and TGA approved the largest proportion of NASs where the submission occurred following first-in-world approval (type 3). In general, type 1 products had the longest approval time, except for Health Canada, as well as TGA which did not approve any NASs that were unique to Australia. For Swissmedic and PMDA, type 3 NASs had the shortest approval time, which may indicate that those agencies are perhaps leveraging what is known about the compound during review.

**In the past decade, agencies have been putting initiatives in place in order to improve the quality and timeliness of the review. This may explain the general decrease and convergence in the approval times seen amongst the six agencies. One area agencies have been concentrating on is improvement of the company submissions ahead of the review in order to ensure that target review timelines are met (Figure 15).** This includes: pre-submission activities – which vary from administrative activities to those that start reviewing the dossier and validation activities in order to further assess the quality of submission prior to assessment, such as the pre-PDUFA filing 2-month review. Finally, agencies may have other administrative time, such as the EMA European Commission or PMDA Ministry of Health, Labour and Welfare ahead of final approval. Such activities further improve consistency and predictability of the review, but have also impacted the overall approval time either in a positive or negative manner as seen in the last decade.

Figure 15: 'Pre-submission meeting,' 'validation' and 'licensing decision and administrative' time activities for six authorities

| | Pre-submission meeting **(timing before submission)** | Validation **(duration)** | Licensing decision and administrative time **(duration)** |
|---|---|---|---|
| | Pre-submission meeting (**7 months**) | Validation (13 WD = 19 CD = **0.6 months**) | European Commission and translation (67 days = **2.2 months**) |
| | Pre-NDA (**6 months**) | Pre-PDUFA filing review (60 CD = **2 months**) | - |
| | Pre-submission consultation (prior assessment) (**6 months**) | - | Ministry of Health, Labour and Welfare meeting and approval stamp (approx. **1.5-2 months**) |
| | Pre-submission meeting (timing not specified in the public domain) | Validation phase (55 CD = **1.8 months**) | - |
| | Pre-submission (**6 months**) | Validation (30 CD = **1 month**) | - |
| | Mandatory pre-submission planning form (**2.25 months**) | Validation (40 WD = 58 CD = **1.9 months**) | - |

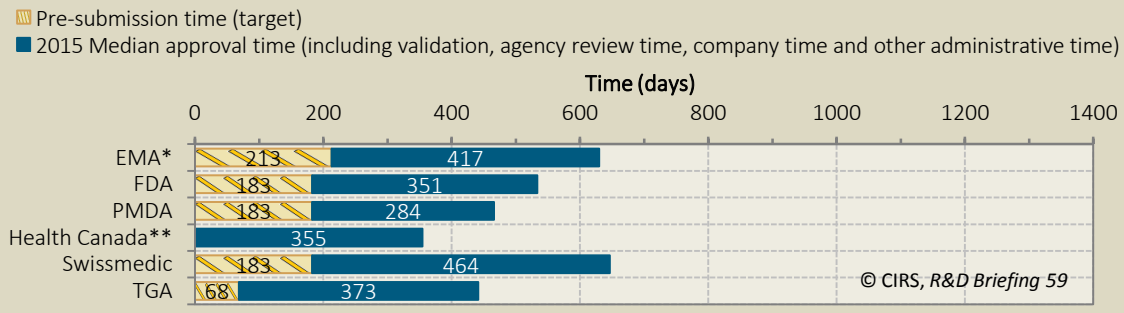
Regulatory Review



CD = Calendar days; WD = Working days

**It is therefore important that as companies plan their submissions, they take these various additional pre-submission timelines into consideration in order to meet expectations and increase predictability (Figure 16). Nevertheless, it should be noted that these meetings are in general not mandatory and not all products will go through these routes.** Finally, further opportunities to asses the breakdown of approval time into validation, company time and other administrative time will have the potential to uncover where time is spent and where efforts can be placed to decrease overall approval time.

Figure 16: Median time to approval (days) in 2015 and target duration of pre-submission activities for six regulatory authorities




*The EMA approval time includes the EU Commission time.

**Health Canada does offer pre-submission meetings, but has not specified their recommended timings.



# Approval at EMA 2015



EMA **APPROVED A TOTAL OF 41 NASs IN 2015** WITH A MEDIAN APPROVAL TIME OF **417 DAYS***

**THE MEDIAN EU COMMISSION TIME WAS 60 DAYS, THE AGENCY TIME 242 DAYS AND COMPANY TIME 110 DAYS**

## Type of Medicine

**15 BIOLOGIC NASs APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **408 DAYS**

**26 CHEMICAL NASs APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **428 DAYS**

**13 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **428 DAYS**

**28 NASs IN OTHER THERAPY AREAS APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **417 DAYS**

## Designation and Review Type

**8 EXPEDITED** NAS APPROVALS IN 2015** WITH A MEDIAN APPROVAL TIME OF **282 DAYS,** THIS IS A MEDIAN **164 DAYS FASTER** THAN THE **33 STANDARD NAS APPROVALS IN 2015**

**15 ORPHAN NAS APPROVALS IN 2015** WITH A MEDIAN APPROVAL TIME OF **453 DAYS,** THIS IS A MEDIAN **37 DAYS SLOWER** THAN THE **26 NON-ORPHAN NAS APPROVALS IN 2015**

## Availability in EMA

**24% OF THE NASs APPROVED IN 2015 BY EMA** WERE APPROVED BY EMA **FIRST OR WITHIN ONE MONTH OF THEIR FIRST APPROVAL AT FDA, PMDA, HEALTH CANADA, SWISSMEDIC OR TGA**

**76% OF THE NASs APPROVED IN 2015 BY EMA** WERE APPROVED AT FDA, PMDA, HEALTH CANADA, SWISSMEDIC OR TGA **FIRST OR MORE THAN ONE MONTH BEFORE BEING APPROVED IN EMA**

THE MEDIAN **SUBMISSION GAP*** ** TO EMA FOR THESE NASs WAS **60 DAYS**

*The EMA approval time includes the EU Commission time.

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

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

# Approval at FDA 2015



FDA *(CDER AND CBER)* **APPROVED A TOTAL OF 51 NASs IN 2015** WITH A MEDIAN APPROVAL TIME OF **351 DAYS**

**FOR THE 45 NASs APPROVED BY CDER, 87% WERE 1-CYCLE REVIEWS, 9% 2-CYCLE , 4% >3-CYCLE**

## Type of Medicine

**18 BIOLOGIC NASs APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **356 DAYS**

**33 CHEMICAL NASs APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **336 DAYS**

**17 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **301 DAYS**

**34 NASs IN OTHER THERAPY AREAS APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **364 DAYS**

## Designation and Review Type

**27 EXPEDITED* NAS APPROVALS IN 2015** WITH A MEDIAN APPROVAL TIME OF **242 DAYS,** THIS IS A MEDIAN **123 DAYS FASTER** THAN THE **24 STANDARD NAS APPROVALS IN 2015**

**26 ORPHAN NAS APPROVALS IN 2015** WITH A MEDIAN APPROVAL TIME OF **333 DAYS,** THIS IS A MEDIAN **32 DAYS FASTER** THAN THE **25 NON-ORPHAN NAS APPROVALS IN 2015**

## Availability in FDA

**73% OF THE NASs APPROVED IN 2015 BY FDA** WERE APPROVED BY FDA **FIRST OR WITHIN ONE MONTH OF THEIR FIRST APPROVAL AT EMA, PMDA, HEALTH CANADA , SWISSMEDIC OR TGA**

**27% OF THE NASs APPROVED IN 2015 BY FDA** WERE APPROVED AT EMA, PMDA, HEALTH CANADA, SWISSMEDIC OR TGA **FIRST OR MORE THAN ONE MONTH BEFORE BEING APPROVED IN FDA**

THE MEDIAN **SUBMISSION GAP**** TO FDA FOR THESE NASs WAS **179 DAYS**

*'Expedited review' refers to EMA 'Accelerated Assessment and FDA/PMDA/Health Canada/Swissmedic 'Priority Review'.
**Date of submission at the first regulatory agency to the date of regulatory submission to the target agency.

# Approval at PMDA 2015



PMDA **APPROVED A TOTAL OF 32 NASs IN 2015** WITH A MEDIAN APPROVAL TIME OF **284 DAYS**

## Type of Medicine

**7 BIOLOGIC NASs APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **287 DAYS**

**25 CHEMICAL NASs APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **282 DAYS**

**9 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **273 DAYS**

**23 NASs IN OTHER THERAPY AREAS APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **311 DAYS**

## Designation and Review Type

**15 EXPEDITED* NAS APPROVALS IN 2015** WITH A MEDIAN APPROVAL TIME OF **269 DAYS,** THIS IS A MEDIAN **68 DAYS FASTER** THAN THE **17 STANDARD NAS APPROVALS IN 2015**

**11 ORPHAN NAS APPROVALS IN 2015** WITH A MEDIAN APPROVAL TIME OF **269 DAYS,** THIS IS A MEDIAN **44 DAYS FASTER** THAN THE **21 NON-ORPHAN NAS APPROVALS IN 2015**

## Availability in PMDA

**34% OF THE NASs APPROVED IN 2015 BY PMDA** WERE APPROVED IN PMDA **FIRST OR WITHIN ONE MONTH OF THEIR FIRST APPROVAL AT EMA, FDA, HEALTH CANADA, SWISSMEDIC OR TGA**

**66% OF THE NASs APPROVED IN 2015 BY PMDA** WERE APPROVED AT EMA, FDA, HEALTH CANADA, SWISSMEDIC OR TGA **FIRST OR MORE THAN ONE MONTH BEFORE BEING APPROVED IN PMDA**

THE MEDIAN **SUBMISSION GAP**** TO PMDA FOR THESE NASs WAS **836 DAYS**

*'Expedited review' refers to EMA 'Accelerated Assessment and FDA/PMDA/Health Canada/Swissmedic 'Priority Review'.
**Date of submission at the first regulatory agency to the date of regulatory submission to the target agency.

# Approval at Health Canada 2015



HEALTH CANADA **APPROVED A TOTAL OF 36 NASs IN 2015** WITH A MEDIAN APPROVAL TIME OF **355 DAYS**

## Type of Medicine

**14 BIOLOGIC NASs APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **366 DAYS**

**22 CHEMICAL NASs APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **354 DAYS**

**13 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **353 DAYS**

**23 NASs IN OTHER THERAPY AREAS APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **356 DAYS**

## Designation and Review Type

**5 EXPEDITED* NAS APPROVALS IN 2015** WITH A MEDIAN APPROVAL TIME OF **277 DAYS,** THIS IS A MEDIAN **102 DAYS FASTER** THAN THE **31 STANDARD NAS APPROVALS IN 2015**

*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 HC IN 2015** WITH A MEDIAN APPROVAL TIME OF **350 DAYS**

## Availability in Health Canada

**11% OF THE NASs APPROVED IN 2015 BY HEALTH CANADA** WERE APPROVED BY HEALTH CANADA **FIRST OR WITHIN ONE MONTH OF THEIR FIRST APPROVAL AT EMA, FDA, PMDA, SWISSMEDIC OR TGA**

**89% OF THE NASs APPROVED IN 2015 BY HEALTH CANADA** WERE APPROVED AT EMA, FDA, PMDA, SWISSMEDIC OR TGA **FIRST OR MORE THAN ONE MONTH BEFORE BEING APPROVED IN HEALTH CANADA**

THE MEDIAN **SUBMISSION GAP**** TO HEALTH CANADA FOR THESE NASs WAS **198 DAYS**

*'Expedited review' refers to EMA 'Accelerated Assessment and FDA/PMDA/Health Canada/Swissmedic 'Priority Review'.
**Date of submission at the first regulatory agency to the date of regulatory submission to the target agency.

# Approval at Swissmedic 2015



SWISSMEDIC **APPROVED A TOTAL OF 27 NASs IN 2015** WITH A MEDIAN APPROVAL TIME OF **464 DAYS**

## Type of Medicine

**7 BIOLOGIC NASs APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **464 DAYS**

**20 CHEMICAL NASs APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **454 DAYS**

**16 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **413 DAYS**

**11 NASs IN OTHER THERAPY AREAS APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **553 DAYS**

## Designation and Review Type

**9 EXPEDITED* NAS APPROVALS IN 2015** WITH A MEDIAN APPROVAL TIME OF **230 DAYS,** THIS IS A MEDIAN **309 DAYS FASTER** THAN THE **18 STANDARD NAS APPROVALS IN 2015**

**6 ORPHAN NAS APPROVALS IN 2015** WITH A MEDIAN APPROVAL TIME OF **364 DAYS,** THIS IS A MEDIAN **126 DAYS FASTER** THAN THE **21 NON-ORPHAN NAS APPROVALS IN 2015**

## Availability in Swissmedic

**11% OF THE NASs APPROVED IN 2015 BY SWISSMEDIC** WERE APPROVED BY SWISSMEDIC **FIRST OR WITHIN ONE MONTH OF THEIR FIRST APPROVAL AT FDA, EMA, PMDA, HEALTH CANADA OR TGA**

**89% OF THE NASs APPROVED IN 2015 BY SWISSMEDIC** WERE APPROVED AT FDA, EMA, PMDA, HEALTH CANADA OR TGA **FIRST OR MORE THAN ONE MONTH BEFORE BEING APPROVED IN SWISSMEDIC**

THE MEDIAN **SUBMISSION GAP**** TO SWISSMEDIC FOR THESE NASs WAS **231 DAYS**

*'Expedited review' refers to EMA 'Accelerated Assessment and FDA/PMDA/Health Canada/Swissmedic 'Priority Review'.
**Date of submission at the first regulatory agency to the date of regulatory submission to the target agency.

# Approval at TGA 2015



TGA **APPROVED A TOTAL OF 27 NASs IN 2015** WITH A MEDIAN APPROVAL TIME OF **373 DAYS**

## Type of Medicine

**7 BIOLOGIC NASs APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **309 DAYS**

**20 CHEMICAL NASs APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **383 DAYS**

**14 ANTI-CANCER AND IMMUNOMODULATOR NASs APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **365 DAYS**

**13 NASs IN OTHER THERAPY AREAS APPROVED IN 2015** WITH A MEDIAN APPROVAL TIME OF **382 DAYS**

## Designation and Review Type

**0 EXPEDITED NAS APPROVALS IN 2015** TGA DOES NOT CURRENTLY HAVE AN EXPEDITED EVALUATION PROGRAMME

**6 ORPHAN NAS APPROVALS IN 2015** WITH A MEDIAN APPROVAL TIME OF **369 DAYS,** THIS IS A MEDIAN **4 DAYS FASTER** THAN THE **21 NON-ORPHAN NAS APPROVALS IN 2015**

## Availability in TGA

**4% OF THE NASs APPROVED IN 2015 BY TGA** WERE APPROVED BY TGA **FIRST OR WITHIN ONE MONTH OF THEIR FIRST APPROVAL BY FDA, EMA, PMDA, HEALTH CANADA OR SWISSMEDIC**

**96% OF THE NASs APPROVED IN 2015 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 **194 DAYS**

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

### 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 'Priority Review'. TGA does not currently have an expedited evaluation programme

### 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, 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
- 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

### 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
- 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

*The full list of NASs approved by each jurisdiction in 2015 will be made available on the CIRS website.

# R&D Briefing 59

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