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Table of Contents

LAWINTER REVIEW - Volume 17– nº 01 – 2026

Special edition - Guest Editors of the Current Issue

Professors Daniel Freire e Almeida and Verônica Scriptore

*La densification procédurale de la due diligence climatique:
vers un contrôle juridictionnel de la mise en œuvre des
obligations climatiques internationales*

ADRIANA FREISLEBEN DE ZANETTI

DANIEL FREIRE E ALMEIDA

..... **11**

*The Evolution of the Regulation of Artificial Intelligence in
Medicine: A Comparative Perspective Among Brazil, Europe,
and the United States*

GABRIELA MARIA DE ALMEIDA TEIXEIRA

VERÔNICA SCRIPTORE FREIRE E ALMEIDA

..... **47**

***European integration as a model of political and economic
development oriented towards globalization***

CAROLINA APARECIDA GALVANESE DE SOUSA

DANIEL FREIRE E ALMEIDA

LUIZ SALES DO NASCIMENTO

..... 83

***Regulation of disease-modifying treatments for Alzheimer’s
disease: a comparative study between the United States and
Brazil***

CÉLIO RAMOS FARIAS

VERÔNICA SCRIPTORE FREIRE E ALMEIDA

MARCELO LAMY

.. 119

Adriana Freisleben de Zanetti - Daniel Freire e Almeida

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LA DENSIFICATION PROCÉDURALE DE LA DUE DILIGENCE CLIMATIQUE: VERS UN CONTRÔLE JURIDICTIONNEL DE LA MISE EN ŒUVRE DES OBLIGATIONS CLIMATIQUES INTERNATIONALES ¹

Adriana Freisleben de Zanetti ^{2*}

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La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

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Résumé

L'article examine les effets des avis consultatifs rendus entre 2024 et 2025 par le Tribunal international du droit de la mer, la Cour interaméricaine des droits de l'homme et la Cour internationale de justice sur les obligations des États en matière climatique. Il soutient que ces avis favorisent un processus de densification procédurale de la due diligence climatique, en élargissant les critères juridiques d'appréciation de l'action étatique et en rendant progressivement plus exigeante la norme de comportement attendue des États.

Mots-clés: Due diligence; Avis consultatifs internationaux; Densification procédurale; Contentieux climatique.

1. Introduction

Le présent article examine les effets de la récente production consultative internationale sur l'interprétation des obligations étatiques de due diligence en matière climatique. L'analyse se concentre sur les avis consultatifs rendus entre 2024 et 2025 par le Tribunal international du droit de la mer, la Cour interaméricaine des droits de l'homme et la Cour internationale de justice, afin

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**La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales**

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d'identifier dans quelle mesure ces prises de position contribuent à redéfinir les critères juridiques d'appréciation du comportement des États face aux risques climatiques.

Le sujet revêt une importance particulière au regard des difficultés à intégrer la crise climatique dans les catégories traditionnelles du droit international. La construction classique de la responsabilité s'est développée autour de relations relativement délimitables entre conduite, dommage et imputation à l'État, dans des contextes où il était davantage possible d'individualiser les contributions causales et de circonscrire les effets dans l'espace et dans le temps. Le contentieux climatique introduit, toutefois, des difficultés supplémentaires: les effets des changements climatiques résultent de l'accumulation de conduites multiples, se déploient dans le temps et dépassent fréquemment les frontières territoriales et institutionnelles, ce qui accroît l'importance des obligations orientées vers la prévention et la gestion continue des risques.

Dans ce contexte, le devoir de due diligence occupe une place centrale. Traditionnellement comprise comme une obligation de comportement variable selon le contexte réglementaire et les capacités des États, la diligence internationale est aujourd'hui réinterprétée à la lumière d'exigences liées à la prévention, à

**La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales**

DOI: <https://doi.org/10.5281/zenodo.23067527>

l'intégration des connaissances scientifiques et au suivi continu des réponses étatiques aux risques climatiques. La question juridique se déplace ainsi de la simple identification du fait internationalement illicite vers les critères utilisés pour apprécier le caractère suffisant du comportement de l'État.

Les avis consultatifs récents offrent un terrain particulièrement pertinent pour observer ce processus. Bien qu'ils s'inscrivent dans des cadres normatifs différents, ils convergent en attribuant une plus grande densité aux obligations climatiques internationales et en élargissant les éléments juridiquement pertinents pour apprécier la diligence étatique. La mise en œuvre de mesures réglementaires, la prise en compte des meilleures données scientifiques disponibles, l'actualisation périodique des réponses institutionnelles et la continuité de l'action publique acquièrent ainsi un rôle plus marqué dans l'interprétation des obligations, révélant un processus de densification procédurale de la due diligence climatique. L'hypothèse défendue est que la nouveauté de cette évolution ne réside pas seulement dans l'intensification du degré de diligence exigé des États, mais dans l'intégration progressive des processus de mise en œuvre, de justification, de révision et de supervision au contenu juridiquement appréciable de

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

l'obligation elle-même. C'est ce déplacement que le présent article qualifie de densification procédurale de la due diligence climatique.

Le présent article est structuré en cinq parties. Il présente d'abord brièvement la due diligence et son rapport au contexte climatique. Il examine ensuite les avis consultatifs et leurs effets sur la configuration contemporaine des obligations climatiques internationales. Il analyse ensuite les éléments de rationalité administrative présents dans ce processus interprétatif. Puis il étudie le rapprochement entre contentieux climatique et mécanismes de supervision de la mise en œuvre étatique. Enfin, il examine la construction de paramètres procéduraux applicables à la mise en œuvre des obligations climatiques internationales.

2. La due diligence climatique

La *due diligence*⁴ s'est consolidée comme une catégorie destinée à apprécier le comportement de l'État face aux situations

⁴ La formulation doctrinale du concept de due diligence climatique revient, dans le domaine des entreprises et des droits humains, à MACCHI, Chiara. *The climate change dimension of business and human rights: the gradual consolidation of a concept of 'climate due diligence'*. Business and Human Rights Journal, Cambridge, v. 6, n. 1, p. 93-119, févr. 2021. L'auteure soutient que la due diligence en matière de droits humains, telle que consacrée par les Principes directeurs des Nations Unies relatifs aux entreprises et aux droits de l'homme (2011), doit être interprétée de manière large, en intégrant les impacts

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

de risque. Son développement a été associé à la nécessité d'élaborer des critères juridiques d'attribution de responsabilité dans les hypothèses où l'État n'était pas directement à l'origine du dommage, mais disposait d'une capacité de surveillance, de réglementation ou de contrôle sur des activités potentiellement préjudiciables.

Il s'agit d'un concept variable et contextuel, dont le contenu n'est pas déterminé à l'avance mais construit en fonction du risque réglementé et de la norme de prudence juridiquement attendue⁵. La consolidation de ce modèle s'est opérée dans des contextes

climatiques comme dimension intrinsèque de la responsabilité des entreprises de respecter les droits humains. En droit international public, constitue une contribution importante l'étude de VIÑUALES, Jorge E. *Due diligence in international environmental law: a fine-grained cartography*. In: KRIEGER, Heike; PETERS, Anne; KREUZER, Leonhard (dir.). *Due diligence in the international legal order*. Oxford: Oxford University Press, 2020. p. 111-128. Viñuales cartographie les fondements normatifs du devoir de due diligence en droit international de l'environnement, analyse qui éclaire, sur un plan plus concret, son activité de conseil juridique auprès de la République de Vanuatu dans la procédure ayant conduit à l'avis consultatif de la Cour internationale de Justice sur le changement climatique (2025), dans lequel la due diligence climatique a été reconnue comme une obligation coutumière contraignante pour les États, couvrant également la réglementation des acteurs privés.

⁵ VIÑUALES, Jorge E. *Due diligence in international environmental law: a fine-grained cartography*. In: KRIEGER, Heike; PETERS, Anne; KREUZER, Leonhard (dir.). *Due diligence in the international legal order*. Oxford: Oxford University Press, 2020. p. 111-128, p. 116-117.

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

caractérisés par une plus grande possibilité de délimiter les dommages et d'individualiser les conduites pertinentes⁶.

Dans le domaine environnemental, la *due diligence* a progressivement été rattachée au principe de prévention des dommages significatifs, aux évaluations d'impact environnemental et à l'intégration des meilleures connaissances scientifiques disponibles dans les décisions réglementaires, la jurisprudence internationale ayant incorporé de nouveaux éléments dans l'appréciation de la régularité de la conduite étatique⁷.

⁶ Sur la consolidation de la diligence environnementale comme technique réglementaire associée à la gestion des risques et à l'adaptation institutionnelle face à l'incertitude, voir VIÑUALES, Jorge E. *The Organisation of the Anthropocene: In Our Hands?* <https://doi.org/10.17863/CAM.26835>. Consulté le 01/05/2026.

⁷ La consolidation de la *due diligence* comme paramètre d'appréciation du comportement étatique en matière environnementale traverse toute l'histoire du droit international de l'environnement. Dans l'affaire *Trail Smelter* (États-Unis c. Canada), tranchée en deux étapes en 1938 et 1941, le Tribunal arbitral spécial a établi qu'aucun État n'a le droit d'utiliser ou de permettre l'utilisation de son territoire de manière à causer des dommages au territoire d'un autre État, posant ainsi les bases de la règle interdisant de causer un dommage transfrontière significatif en tant qu'obligation de droit international coutumier (TRIBUNAL ARBITRAL SPÉCIAL. *Trail Smelter Case* (United States v. Canada). Reports of International Arbitral Awards, v. III, p. 1905-1982, 11 mars 1941. Disponible sur: https://legal.un.org/riaa/cases/vol_III/1905-1982.pdf. Consulté le 2 juin 2025. Dans l'affaire *Pulp Mills on the River Uruguay* (Argentina v. Uruguay), la CIJ a reconnu l'évaluation de l'impact environnemental transfrontière comme une obligation de droit international général et réaffirmé que les États ont le devoir d'agir avec la diligence requise afin de prévenir les dommages à l'environnement

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

Les défis environnementaux et les changements climatiques ont imposé l'adaptation du modèle traditionnel de responsabilité à de nouvelles exigences opérationnelles. Les questions liées à la causalité complexe et à la distribution transnationale des impacts ont déplacé l'attention, de la reconstruction rétrospective du dommage, vers la capacité institutionnelle d'anticiper, d'organiser et de gérer les risques probables. L'effectivité du régime climatique dépend désormais moins de l'imposition uniforme de résultats que du maintien de structures permanentes de révision et de coordination réglementaire⁸.

partagé (COUR INTERNATIONALE DE JUSTICE - CIJ. *Pulp Mills on the River Uruguay*. Arrêt du 20 avril 2010. ICJ Reports, p. 14, 2010). Disponible sur: <https://www.icj-cij.org/case/135>. Consulté le 2 juin 2025. Au sein du Tribunal International du Droit de la Mer, la Chambre pour le règlement des différends relatifs aux fonds marins a rendu, le 1er février 2011, un avis consultatif sur les responsabilités et obligations des États qui patronnent des activités dans la Zone, précisant que l'obligation d'adopter des règles et mesures appropriées constitue une obligation de comportement guidée par la *due diligence*, laquelle exige une surveillance continue et un contrôle administratif des opérateurs relevant de leur juridiction (TRIBUNAL INTERNATIONAL DU DROIT DE LA MER. Chambre pour le règlement des différends relatifs aux fonds marins. *Responsibilities and Obligations of States Sponsoring Persons and Entities with Respect to Activities in the Area*. Avis consultatif n° 17, 1er févr. 2011. Disponible sur: <https://www.itlos.org/en/main/cases/list-of-cases/case-no-17/>. Consulté le 2 juin 2025.

⁸ En ce sens, Lavanya Rajamani identifie un déplacement de l'axe traditionnel des obligations climatiques vers des mécanismes itératifs de mise en œuvre, d'actualisation périodique et de suivi continu des mesures adoptées par les États.

**La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales**

DOI: <https://doi.org/10.5281/zenodo.23067527>

On observe actuellement une densification procédurale de la *due diligence* climatique: l'institution intègre désormais des exigences relatives à la science, à la révision périodique des politiques publiques, à la justification technique des décisions réglementaires et à l'existence de capacités institutionnelles aptes à suivre l'évolution des risques climatiques. L'objet de l'évaluation juridique cesse de se concentrer exclusivement sur la mesure adoptée et englobe les processus par lesquels les décisions publiques sont élaborées, mises en œuvre et révisées, comme le montre l'analyse des avis consultatifs rendus entre 2024 et 2025.

3. La densification procédurale de la due diligence climatique

Les avis rendus entre 2024 et 2025 permettent d'observer comment des obligations déjà consolidées en droit international sont interprétées et appliquées dans des situations caractérisées par des risques climatiques de longue durée, une causalité hautement complexe et une forte dépendance à l'égard des connaissances technico-scientifiques. L'intérêt de la présente

In: RAJAMANI, Lavanya. *Due diligence in international climate change law*. KRIEGER, Heike; PETERS, Anne; KREUZER, Leonhard (dir.). *Due diligence in the international legal order*. Oxford: Oxford University Press, 2020. p. 160-178.

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

analyse réside dans les critères utilisés par les juridictions pour apprécier le respect des obligations étatiques et dans les éléments qui intègrent désormais le contenu opérationnel de la diligence internationale.

3.1. L'avis du Tribunal international du droit de la mer – TIDM (2024)

Le 21 mai 2024, le TIDM a rendu son avis consultatif sur les obligations des États au titre de la Convention des Nations Unies sur le Droit de la Mer (CNUDM), en réponse à la demande de la Commission des petits États insulaires sur le changement climatique et le droit international.

Le point de départ interprétatif du Tribunal a consisté à qualifier juridiquement les émissions anthropiques de gaz à effet de serre de forme de pollution du milieu marin au sens de l'article 1, paragraphe 1, point 4, de la CNUDM. En reconnaissant que l'acidification, le réchauffement et les autres altérations physico-chimiques résultant de ces émissions produisent des effets néfastes sur les écosystèmes marins, le TIDM a intégré le risque climatique dans le cadre déjà consolidé de protection et de préservation du milieu marin prévu par la partie XII de la Convention.

**La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales**

DOI: <https://doi.org/10.5281/zenodo.23067527>

La conséquence juridique la plus significative a résidé dans la qualification du degré de diligence exigé. Au paragraphe 257 de l’avis, le Tribunal a affirmé que l’obligation de due diligence applicable aux émissions de gaz à effet de serre est rigoureuse, compte tenu de la gravité et de l’irréversibilité des dommages causés au milieu marin identifiés par les rapports du Groupe d’experts intergouvernemental sur l’évolution du climat⁹. Le paragraphe 232 est tout aussi pertinent. Le Tribunal a déterminé que le respect de l’article 194 de la CNUDM exige des États qu’ils adoptent un cadre réglementaire effectif pour réduire les émissions de gaz à effet de serre et qu’ils l’appliquent effectivement. Dès lors, la législation interne, les mécanismes administratifs, les instruments de contrôle et la capacité d’exécution coercitive intègrent l’examen juridique du caractère suffisant de l’action étatique.

Un autre élément important tient à la centralité accordée à la science. Aux paragraphes 219 à 224, le Tribunal a utilisé les rapports du GIEC comme référence pour délimiter les risques et déterminer

⁹ TRIBUNAL INTERNATIONAL DU DROIT DE LA MER. Avis consultatif du 21 mai 2024. Paragraphe 257 : « an obligation of due diligence can be highly demanding ».

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

le contenu des mesures exigibles. Il ressort du texte que les connaissances scientifiques cessent d'être un élément purement auxiliaire et deviennent un élément important de concrétisation du contenu des obligations.

Il convient toutefois de relever que l'avis du TIDM a également suscité des critiques. Le rejet, par le Tribunal, d'un rapport de lex specialis entre la CNUDM et l'Accord de Paris a été contesté par une partie de la doctrine, qui soutient que cette mise à l'écart a permis au Tribunal d'établir un niveau de diligence plus rigoureux que celui exigé par le régime climatique conventionnel lui-même, sans offrir de critères précis pour résoudre la tension entre les deux régimes¹⁰.

3.2 L'avis consultatif de la Cour interaméricaine des droits de l'homme – Cour IDH (2025)

Le 3 juillet 2025, la Cour IDH a rendu l'avis consultatif OC-32/25¹¹ sur l'urgence climatique et les droits humains, en réponse à une demande conjointe du Chili et de la Colombie. La procédure

¹⁰ KLERK, B. E. *The ITLOS advisory opinion on climate change: revisiting the relationship between the United Nations Convention on the Law of the Sea and the Paris Agreement*. *Review of European, Comparative & International Environmental Law*. Oxford, v. 34, n. 2, p. 181-195, 2025.

¹¹ COUR INTERAMÉRICAINNE DES DROITS DE L'HOMME. Avis consultatif OC-32/25. San José, 3 juill. 2025.

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

a donné lieu à des audiences à la Barbade, à Brasília et à Manaus, avec la participation d'organisations sociales, de communautés autochtones et de groupes directement touchés par les impacts climatiques.

L'avis appréhende l'urgence climatique sous l'angle des droits humains, avec des conséquences directes sur la compréhension de la due diligence étatique. À la différence du TIDM, qui a travaillé à partir de la notion de pollution du milieu marin, la Cour IDH part des obligations positives découlant de l'article 1, paragraphe 1, de la Convention américaine relative aux droits de l'homme pour délimiter les obligations climatiques des États.

L'élément central a consisté dans l'introduction d'un niveau de *due diligence* "renforcée". Se fondant sur le niveau de risque identifié par la science du climat et sur la vulnérabilité des groupes concernés, la Cour a affirmé que les États ont l'obligation d'adopter toutes les mesures appropriées pour réduire les risques découlant de la dégradation du système climatique. Selon la Cour, le degré de diligence exigé est proportionnel au niveau de risque, au type de mesures requises et à la vulnérabilité des personnes affectées, ce qui implique un degré de responsabilité plus intense dans les situations de plus forte exposition.

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

Dans les paragraphes relatifs aux obligations générales dans le contexte de l'urgence climatique, la Cour a associé le respect des obligations étatiques au maintien de processus visant à produire de l'information environnementale, à développer des capacités d'identification et de suivi des risques et à intégrer les groupes concernés au processus décisionnel. Les droits d'accès à l'information, de participation du public et de transparence occupent ainsi une place directement liée à la mise en œuvre des obligations climatiques. L'avis utilise ces éléments comme instruments destinés à assurer la continuité, le contrôle et la révisabilité de l'action étatique.

Un autre aspect mérite d'être souligné : la manière dont l'avis a traité la relation entre l'action de l'État et les activités privées.

La Cour a établi le devoir des États d'exiger des entreprises privées qu'elles exercent une due diligence tout au long de leurs processus de production, en identifiant, prévenant et atténuant les impacts négatifs sur les droits humains et l'environnement. En ce sens, l'action étatique intégrerait une dimension organisationnelle liée à la construction d'environnements réglementaires capables d'identifier les risques, d'établir des normes de conduite et de

**La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales**

DOI: <https://doi.org/10.5281/zenodo.23067527>

superviser en permanence les activités économiques ayant un impact climatique significatif.

La Cour a également intégré la perspective intergénérationnelle aux obligations climatiques: aux paragraphes 155 à 157 de l'avis, la Cour reconnaît que les États sont tenus d'obligations non seulement envers les générations présentes, mais aussi envers les générations futures. La continuité de l'action étatique est ainsi examinée comme un élément de la mise en œuvre même des obligations internationales et renforce l'interprétation selon laquelle un comportement diligent exige le maintien de capacités permanentes de réponse et d'adaptation institutionnelle.

Il convient encore de mentionner que le processus participatif ayant précédé l'avis ne constituait pas seulement une dimension procédurale formelle. La Cour a expressément utilisé les témoignages de communautés autochtones, de populations côtières et de groupes affectés pour fonder son interprétation de la vulnérabilité différenciée et de l'étendue des devoirs étatiques. La participation a ainsi fonctionné comme un mécanisme d'intégration de connaissances distribuées dans le contenu interprétatif de l'avis.

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

3.3 L’avis consultatif de la Cour internationale de justice – CIJ (2025)

Le 23 juillet 2025, la CIJ a rendu son avis consultatif sur les obligations des États à l’égard des changements climatiques¹², en réponse à la demande de l’Assemblée générale des Nations Unies.

L’avis a articulé le régime climatique conventionnel — notamment la Convention-cadre des Nations Unies sur les changements climatiques, le Protocole de Kyoto et l’Accord de Paris — avec les principes du droit international coutumier, en proposant un traitement intégré des obligations climatiques. L’aspect le plus pertinent a été la reconnaissance d’une obligation contraignante des États de prévenir les dommages significatifs au système climatique.

Au paragraphe 282, la CIJ a affirmé que la due diligence climatique exige des États qu’ils adoptent des mécanismes réglementaires d’atténuation destinés à parvenir à des réductions profondes, rapides et durables des émissions de gaz à effet de serre. Selon la Cour, ces mécanismes doivent refléter les données

¹² COUR INTERNATIONALE DE JUSTICE. Avis consultatif sur les obligations des États à l’égard des changements climatiques. La Haye, 23 juill. 2025. *Obligations of States in respect of climate change, Advisory Opinion*, 2025 I.C.J. Consulté le 27 mai 2026.

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

scientifiques disponibles, les normes pertinentes — y compris les décisions des Conférences des Parties — et le principe des responsabilités communes mais différenciées. Dans le prolongement de l’avis du TIDM, la CIJ a confirmé que les rapports du GIEC constituent la référence scientifique la plus autorisée pour délimiter ces obligations.

Aux paragraphes 427 et 428, la Cour a directement abordé la question de la réglementation des acteurs privés. Elle a considéré que la responsabilité de l’État ne résulte pas de sa conduite directe dans la production d’émissions, mais de son manquement à exercer la due diligence lorsqu’il omet d’adopter les mesures réglementaires et législatives nécessaires pour limiter les émissions produites par les acteurs privés relevant de sa juridiction.

Aux paragraphes 155 à 157, la Cour a confirmé la dimension intergénérationnelle des obligations: les États sont débiteurs de devoirs de protection du climat non seulement envers les générations présentes, mais également envers les générations futures, formulation qui élargit considérablement la portée temporelle de la *due diligence*.

L’avis de la CIJ a également introduit un élément spécifique relatif à la notification et à la consultation: selon la Cour, ces

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

mécanismes font partie du contenu de la due diligence et sont particulièrement exigibles lorsqu'une activité déterminée affecte de manière significative les efforts collectifs de réduction des dommages au système climatique. Les décisions gouvernementales relatives à l'exploitation de ressources associées aux émissions de gaz à effet de serre, telles que l'octroi ou le refus d'autorisations pour des activités d'extraction de pétrole et de gaz, sont expressément citées comme des situations dans lesquelles cette obligation de consultation s'impose.

3.4 Convergences et tensions

La lecture conjointe des trois avis révèle une convergence quant au noyau normatif de la *due diligence*: les États ont l'obligation d'adopter et de mettre effectivement en œuvre des cadres réglementaires visant à réduire les émissions, fondés sur les meilleures données scientifiques disponibles, périodiquement révisés et assortis d'une capacité institutionnelle de mise en œuvre continue. Aucun des trois avis ne transforme la due diligence en obligation de résultat; tous la maintiennent comme obligation de comportement, mais avec un contenu procédural progressivement plus dense.

La densification procédurale de la due diligence climatique: vers un contrôle juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

Les différences entre les avis sont toutefois tout aussi pertinentes. Le TIDM emploie le langage de la pollution marine et insiste sur la nécessité d'une mise en œuvre coercitive effective du cadre réglementaire; la Cour IDH intègre une perspective de droits humains, de vulnérabilité différenciée et d'intergénérationnalité; la CIJ adopte une approche de droit international général, articulant le régime climatique avec le droit coutumier et avec la responsabilité de l'État pour omission réglementaire. Chacun de ces avis approfondit une dimension particulière de la *due diligence*, sans qu'il existe encore de synthèse pleinement articulée entre eux.

4. Le droit administratif global et les instruments procéduraux de mise en œuvre des obligations climatiques internationales

La densification procédurale identifiée dans les avis précédents rapproche le débat climatique des catégories développées par le droit administratif global – DAG¹³. Le recours au droit administratif

¹³ La formulation centrale de ce champ, développée par Kingsbury, Krisch et Stewart, se concentre sur les procédures qui organisent l'exercice de fonctions réglementaires au sein de structures composées de multiples centres de décision et de processus permanents de mise en œuvre. In: KINGSBURY, Benedict; KRISCH, Nico; STEWART, Richard B. The emergence of global administrative law. *Law and Contemporary Problems*, Durham, v. 68, n. 3, p. 15-61, 2005.

**La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales**

DOI: <https://doi.org/10.5281/zenodo.23067527>

global ne vise pas à subsumer la due diligence climatique dans cette construction théorique, mais à mobiliser ses catégories comme instruments d'analyse permettant d'identifier plus précisément les transformations procédurales qui affectent le contenu opérationnel de l'obligation.

Quatre catégories méritent une attention particulière: la participation des personnes affectées, la motivation juridiquement et techniquement étayée, la révisabilité et la supervision continue.

La participation des personnes affectées correspond à l'intégration institutionnalisée des sujets touchés par les décisions réglementaires dans le processus de formation et de mise en œuvre de ces décisions. Sa fonction ne se limite pas à accroître la représentativité formelle: les procédures participatives élargissent la circulation de l'information, réduisent les asymétries de connaissance et permettent d'intégrer au processus décisionnel les situations concrètes de vulnérabilité. La procédure ayant précédé l'OC-32/25 de la Cour IDH illustre ce mécanisme en pratique. En effet, la participation de communautés autochtones, de populations côtières et de groupes directement touchés n'a pas été seulement symbolique, mais a directement influencé le contenu interprétatif de l'avis.

**La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales**

DOI: <https://doi.org/10.5281/zenodo.23067527>

La motivation juridiquement et techniquement étayée correspond à l'exigence d'explicitier les fondements juridiques, techniques et factuels qui soutiennent une décision donnée. Dans les trois avis analysés, les connaissances scientifiques cessent de fonctionner uniquement comme une référence externe et intègrent le contenu justificatif des décisions juridiques. Le caractère suffisant de l'action étatique dépend également de la démonstration des critères utilisés pour sélectionner les mesures réglementaires, interpréter les risques et définir les priorités de mise en œuvre.

La révisabilité organise des procédures destinées à la réévaluation continue des mesures adoptées face à l'évolution des circonstances factuelles et des connaissances disponibles. Cette catégorie dialogue avec la manière dont les avis traitent la due diligence climatique: l'action étatique cesse d'être examinée à un moment isolé et implique désormais une capacité continue d'actualisation des réponses réglementaires.

La supervision continue correspond au maintien de mécanismes permanents de suivi de la mise en œuvre. Dans le contexte climatique, elle se manifeste par des instruments de

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

notification, une production continue de données et une coordination entre différents niveaux institutionnels.

Les trois avis accordent une importance croissante au maintien de ces capacités comme élément de la due diligence de l'État. Le DAG présente toutefois des limites en tant qu'instrument de gouvernance climatique.

La première critique est d'ordre descriptif: le DAG a été conçu pour décrire des structures réglementaires déjà existantes à l'échelle mondiale, telles que les organisations internationales, les réseaux de régulateurs nationaux, les régimes hybrides public-privé et autres. Or, le problème climatique n'est pas seulement un problème d'organisation et de procédure des structures existantes; il est fondamentalement un problème de production d'obligations substantielles suffisamment denses pour induire des transformations structurelles. En ce sens, l'accent procédural peut, paradoxalement, détourner l'attention de l'insuffisance matérielle des réponses étatiques au risque climatique — le processus, initialement conçu comme un moyen, tend ainsi à devenir une fin en soi¹⁴.

¹⁴ Le droit administratif global, dans sa formulation initiale, a été développé comme un instrument descriptif et normatif consacré aux structures

**La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales**

DOI: <https://doi.org/10.5281/zenodo.23067527>

La deuxième critique concerne la légitimité: en privilégiant les mécanismes de participation et de transparence, le DAG suppose que l'amélioration des procédures constitue une condition suffisante pour produire des décisions réglementaires légitimes et effectives. Dans le domaine climatique, cette prémisse est discutable. Les États et les entreprises fortement émetteurs disposent de la capacité d'influencer les processus participatifs et de justification en faveur de leurs intérêts, sans nécessairement accroître le caractère suffisant de la réponse au risque climatique¹⁵.

réglementaires déjà existantes au niveau international, notamment les organisations intergouvernementales, les réseaux de régulateurs et les régimes hybrides. Dans cette perspective, ses promoteurs reconnaissent que le champ se concentre sur les règles procédurales et les mécanismes de contrôle, et non sur le contenu substantiel des normes produites par les entités réglementaires globales (KINGSBURY, Benedict; KRISCH, Nico; STEWART, Richard B. *The emergence of global administrative law*. Law and Contemporary Problems, v. 68, n. 3-4, p. 15-61, 2005). La tension entre l'accent procédural et l'insuffisance matérielle des réponses réglementaires au risque climatique est relevée par la doctrine spécialisée en droit international du climat, qui observe que les contributions déterminées au niveau national prévues par l'Accord de Paris, bien que soumises à des exigences procédurales contraignantes, n'imposent pas d'obligations substantielles de résultat quant au niveau d'ambition climatique (BODANSKY, Daniel; BRUNNEE, Jutta; RAJAMANI, Lavanya. *International climate change law*. Oxford: Oxford University Press, 2017. p. 198-221; RAJAMANI, Lavanya; BRUNNEE, Jutta. *The legality of downgrading nationally determined contributions under the Paris Agreement: lessons from the US disengagement*. Journal of Environmental Law, v. 29, n. 3, p. 537-551, 2017).

¹⁵ La critique de l'hypothèse selon laquelle l'amélioration procédurale et l'élargissement de la participation constitueraient des conditions suffisantes de

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

La troisième critique est d'ordre structurel: dans sa formulation initiale, le DAG repose sur l'hypothèse que les sujets réglementés et les personnes affectées sont distincts et que les procédures de participation peuvent rapprocher ces groupes. Dans le contexte climatique, cette séparation est plus complexe: tous les États sont simultanément producteurs et victimes du risque climatique, avec des contributions historiques et des capacités de réponse radicalement asymétriques. La logique procédurale ne résout pas les tensions de justice distributive qui structurent le régime climatique international¹⁶.

la légitimité et de l'effectivité des décisions réglementaires a été formulée par Carol Harlow. In: HARLOW, Carol. *Global administrative law: the quest for principles and values*. European Journal of International Law, v. 17, n. 1, p. 187-214, 2006. S'agissant spécifiquement du régime climatique, la doctrine souligne que les processus participatifs peuvent être captés par les intérêts de grands émetteurs. Voir: BODANSKY, Daniel; BRUNNEE, Jutta; RAJAMANI, Lavanya. *International climate change law*. Oxford: Oxford University Press, 2017. p. 147-175). La question de la captation des processus réglementaires globaux par les intérêts organisés d'acteurs puissants est également abordée dans KRISCH, Nico. *The pluralism of global administrative law*. European Journal of International Law, v. 17, n. 1, p. 247-278, 2006.

¹⁶L'asymétrie structurelle entre les États producteurs et les États victimes du risque climatique, ainsi que les implications de la logique procédurale sur les tensions de justice distributive dans le régime climatique international, sont des thèmes centraux de la doctrine du droit international du climat. Le principe des responsabilités communes mais différenciées, consacré à l'article 3, paragraphe 1, de la Convention-cadre des Nations Unies sur les changements climatiques (CCNUCC, 1992) et réaffirmé dans l'Accord de Paris (2015), exprime précisément

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

Cela ne signifie pas que les catégories du DAG soient dépourvues de pertinence pour l'analyse de la *due diligence climatique*. Leur contribution est plutôt partielle: elles permettent de décrire comment des obligations existantes acquièrent une définition opérationnelle plus précise, mais n'expliquent pas pourquoi cette densification procédurale serait suffisante pour faire face aux causes structurelles de la crise climatique.

5. Contentieux climatique et supervision de la mise en œuvre étatique

La densification procédurale de la *due diligence* climatique se répercute sur la manière dont le contentieux climatique

la reconnaissance du fait que tous les États sont à la fois sujets de l'obligation de réponse et affectés à des degrés radicalement asymétriques par le phénomène climatique (RAJAMANI, Lavanya. *Ambition and differentiation in the 2015 Paris Agreement: interpretative possibilities and underlying politics*. International and Comparative Law Quarterly, v. 65, n. 2, p. 493-514, 2016). La limite de la logique procédurale pour résoudre ces tensions distributives est analysée dans BODANSKY, Daniel; BRUNNEE, Jutta; RAJAMANI, Lavanya. *International climate change law*. Oxford: Oxford University Press, 2017. p. 122-146. Dans le cadre plus large de la théorie du droit administratif global, Kingsbury lui-même reconnaît que les mécanismes de participation et de transparence répondent à des valeurs procédurales, mais n'apportent pas de réponse satisfaisante aux valeurs substantielles de nature distributive (KINGSBURY, Benedict; KRISCH, Nico; STEWART, Richard B. *The emergence of global administrative law*. Law and Contemporary Problems, v. 68, n. 3-4, p. 15-61, 2005).

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

contemporain structure l'examen du respect des obligations internationales. Le contrôle juridictionnel intègre de plus en plus les débats sur le caractère suffisant des processus de mise en œuvre, la cohérence entre les engagements pris et les mesures adoptées, ainsi que la qualité de la justification technique des choix réglementaires. Examinons ces éléments.

Dans l'affaire *Urgenda Foundation v. État des Pays-Bas*¹⁷, la Cour suprême des Pays-Bas a confirmé une décision imposant à l'État d'adopter des mesures compatibles avec des paramètres minimaux de réduction des émissions liés à la protection des droits fondamentaux. L'élément décisif n'était pas l'existence d'objectifs climatiques formels, mais l'adéquation de leur mise en œuvre: la Cour a examiné la relation entre les connaissances scientifiques

¹⁷ PAYS-BAS. Cour suprême (Hoge Raad). *Urgenda Foundation c. État des Pays-Bas*. Arrêt du 20 décembre 2019. <https://www.urgenda.nl/wpcontent/uploads/ENG-Dutch-Supreme-Court-Urgenda-v-Netherlands-20-12-2019.pdf>. Consulté le 2 juin 2025. La décision a confirmé l'arrêt de la Cour d'appel de La Haye du 9 octobre 2018 (ECLI:NL:GHDHA:2018:2610), qui avait elle-même confirmé le jugement de première instance du Tribunal de district de La Haye du 24 juin 2015 (Proc. HAZA C/09/00456689). La Cour a examiné la relation entre les connaissances scientifiques disponibles, les engagements pris dans le cadre de la Convention européenne des droits de l'homme (articles 2 et 8) et la capacité de l'État à produire une réponse compatible avec le degré de risque climatique identifié, reconnaissant que l'inadéquation de la mise en œuvre, et non seulement l'absence d'objectifs formels, peut faire l'objet d'un contrôle juridictionnel.

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

disponibles, les engagements internationaux assumés et la capacité de l'État à produire une réponse compatible avec le degré de risque identifié. La structure argumentative révèle un rapprochement entre contentieux climatique et mécanismes de supervision de la mise en œuvre.

Dans l'affaire *Neubauer et autres v. Allemagne*¹⁸, la Cour constitutionnelle fédérale a reconnu que la répartition temporelle des efforts d'atténuation possède une pertinence juridique propre et a conclu que le report excessif des réductions d'émissions entraînait des restrictions futures disproportionnées à l'exercice des libertés. La temporalité de la mise en œuvre devient ainsi objet de contrôle juridictionnel: l'analyse ne se limite pas au caractère immédiatement suffisant de la réponse réglementaire, mais s'étend à la capacité institutionnelle de maintenir les politiques

¹⁸ ALLEMAGNE. Cour constitutionnelle fédérale (Bundesverfassungsgericht). *Neubauer et autres v. République fédérale d'Allemagne*. Décision du Premier Sénat du 24 mars 2021. Disponible sur: http://www.bverfg.de/e/rs20210324_1bvr265618en.html. Consulté le 2 juin 2025. La Cour a déclaré partiellement inconstitutionnelle la loi fédérale de 2019 sur la protection du climat (Bundesklimaschutzgesetz), au motif qu'elle ne fixait pas de manière suffisamment précise les objectifs de réduction des émissions pour la période postérieure à 2030, reconnaissant que le report disproportionné des efforts d'atténuation impose des restrictions futures aux libertés fondamentales des générations à venir et fait ainsi de la temporalité de la mise en œuvre un objet autonome de contrôle juridictionnel.

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

publiques dans le temps, de répartir adéquatement les coûts réglementaires entre les générations et de préserver une marge d'adaptation face à l'évolution des risques.

Dans l'affaire *Milieudefensie et autres v. Royal Dutch Shell*¹⁹, le tribunal néerlandais de première instance a ordonné à l'entreprise d'adopter des objectifs de réduction des émissions compatibles avec l'Accord de Paris. Bien que partiellement réformée en appel, la décision a contribué à consolider la tendance consistant à associer les obligations de réduction des émissions à la nécessité d'élaborer des stratégies continues de mise en œuvre et de justification des choix effectués.

Ces précédents, antérieurs aux avis consultatifs ici analysés, ne sauraient être présentés comme une conséquence de ceux-ci. Ils révèlent plutôt une évolution parallèle du contentieux climatique que les avis de 2024 et 2025 viennent consolider et doter d'un

¹⁹ PAYS-BAS. Tribunal de district de La Haye. *Milieudefensie et autres c. Royal Dutch Shell plc*. Jugement du 26 mai 2021. Affaire n° C/09/571932, HA ZA 19-379. ECLI:NL: RBDHA: 2021:5337. Disponible sur: https://www.climatecasechart.com/document/milieudefensie-et-al-v-royal-dutch-shellplc_c3e4. Consulté le: 2 juin 2025. La décision a été partiellement réformée par la Cour d'appel de La Haye le 12 novembre 2024, qui a écarté l'imposition d'un objectif spécifique de réduction des émissions, tout en reconnaissant que la protection contre les effets dangereux des changements climatiques constitue un droit humain opposable tant aux entités étatiques qu'aux acteurs privés.

**La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales**

DOI: <https://doi.org/10.5281/zenodo.23067527>

fondement international plus articulé. En effet, cette évolution témoigne d'un mouvement plus large de reconfiguration du rôle du contentieux climatique. La décision juridictionnelle s'insère désormais dans des cycles plus étendus de mise en œuvre, de suivi et d'actualisation des mesures adoptées, se rapprochant de modèles de supervision structurelle dans lesquels le jugement ne clôt pas le litige par un acte unique, mais oriente des processus continus d'adaptation institutionnelle.

Les avis consultatifs analysés renforcent et amplifient ce mouvement. La formulation, par le TIDM, la CIJ et la Cour IDH, d'exigences de due diligence au contenu procédural plus dense fournit aux juridictions nationales et internationales des critères plus précis pour examiner l'adéquation de la réponse étatique, non seulement sous l'angle de l'existence formelle de politiques climatiques, mais aussi de la capacité institutionnelle à les maintenir, les réviser et les justifier dans le temps.

Il est toutefois nécessaire de reconnaître les limites de ce modèle. La supervision juridictionnelle de la mise en œuvre suppose que les tribunaux disposent de la légitimité, des capacités techniques et des instruments procéduraux appropriés pour suivre des politiques climatiques de longue durée.

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

6. Paramètres procéduraux de mise en œuvre des obligations climatiques internationales

La lecture des trois avis permet d'identifier un ensemble de paramètres procéduraux qui intègre désormais le contenu opérationnel de la *due diligence* climatique.

La *production continue d'informations* occupe une place centrale. Les inventaires d'émissions, les systèmes de suivi, les indicateurs climatiques et l'évaluation périodique des scénarios acquièrent une fonction juridique élargie: ils rendent l'action étatique observable et permettent de reconstruire le parcours entre les engagements pris et les mesures effectivement exécutées. L'observabilité de la mise en œuvre, comprise comme la possibilité de reconstruire juridiquement le chemin qui relie l'obligation internationale, la décision réglementaire et l'exécution institutionnelle, apparaît comme un élément constitutif du caractère suffisant de la *due diligence*.

La *planification réglementaire en tant que structure de coordination temporelle* est également pertinente. Les plans climatiques, les objectifs progressifs et les processus périodiques de révision remplissent une fonction d'articulation entre les objectifs normatifs et la capacité institutionnelle d'exécution. La stabilité

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

réglementaire, comprise comme une cohérence suffisante pour permettre la coordination et l'anticipation, préserve la capacité de réponse adaptative sans empêcher l'actualisation continue des mesures mises en œuvre.

La *coordination entre les échelles décisionnelles* reflète la nature décentralisée de la mise en œuvre climatique. Les obligations internationales sont opérationnalisées par des structures réparties entre institutions nationales, engagements internationaux et mécanismes permanents de suivi. La capacité de coordination entre ces différentes échelles intègre désormais le contenu de la diligence attendue des États.

La *révisabilité des réponses réglementaires* cesse d'occuper une place résiduelle et s'intègre à la dynamique même de la mise en œuvre. L'actualisation périodique des réponses étatiques permet d'incorporer les évolutions scientifiques, de réorganiser les priorités réglementaires et d'ajuster les instruments précédemment adoptés face à l'évolution des risques.

L'identification de ces paramètres permet de rendre plus intelligible le processus par lequel la *due diligence* climatique acquiert un contenu opérationnel progressivement plus défini. La densification procédurale n'élimine toutefois pas la tension entre

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

obligation juridique et volonté politique. Des États qui produisent des rapports de grande qualité, participent à des procédures consultatives exemplaires et élaborent des plans climatiques sophistiqués peuvent néanmoins adopter des mesures matériellement insuffisantes pour contenir le réchauffement mondial. En outre, la procéduralisation des obligations climatiques peut, dans des cas extrêmes, fonctionner comme un mécanisme de légitimation de politiques climatiques inadéquates, lorsque la conformité formelle aux normes procédurales se dissocie du caractère matériellement suffisant des réponses.

Cette tension n'invalide pas la pertinence du processus de densification identifié dans le présent article. Elle indique toutefois que l'évolution des obligations climatiques internationales se heurte encore à une limite structurelle. Le droit reconnaît désormais plus clairement la dimension persistante et structurelle de l'insuffisance de l'action étatique en matière climatique, mais n'a pas encore développé les instruments capables d'imposer des transformations substantielles dans les choix politiques et économiques qui alimentent la crise.

La densification procédurale de la due diligence climatique: vers un contrôle juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

7. Conclusion

Depuis l'analyse directe des avis consultatifs rendus entre 2024 et 2025, le présent article a identifié un processus de densification procédurale de la due diligence climatique. Les trois avis analysés, du TIDM, de la Cour IDH et de la CIJ, convergent en élargissant les critères au moyen desquels l'action étatique est juridiquement appréciée, sans modifier la nature de l'obligation, qui demeure une obligation de comportement.

Le TIDM a établi que la norme de comportement applicable aux émissions de gaz à effet de serre est rigoureuse en raison de la gravité et de l'irréversibilité des dommages au milieu marin, exigeant un cadre réglementaire effectif et une capacité institutionnelle d'exécution. La Cour IDH a introduit un degré de diligence renforcée, associé à la vulnérabilité différenciée des groupes affectés, et a intégré les droits d'accès à l'information, de participation et de transparence à la structure des obligations climatiques. La CIJ a confirmé, sur le fondement du droit coutumier, l'obligation de prévenir les dommages au système climatique et reconnu la responsabilité de l'État en cas d'omission réglementaire à l'égard des activités d'acteurs privés.

La densification procédurale de la due diligence climatique: vers un contrôle
juridictionnel de la mise en œuvre des obligations climatiques internationales

DOI: <https://doi.org/10.5281/zenodo.23067527>

La densification procédurale identifiée tout au long de l'article montre que la configuration contemporaine des obligations climatiques internationales accorde une centralité croissante aux conditions institutionnelles qui assurent la continuité réglementaire, la coordination entre différentes échelles de décision, l'actualisation permanente des réponses étatiques et la capacité continue d'adaptation face à la transformation des risques climatiques.

Ce mouvement précise les critères au moyen desquels la due diligence climatique est juridiquement appréciée et élargit le rôle joué par les mécanismes de concrétisation dans la configuration contemporaine des obligations internationales.

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La densification procédurale de la due diligence climatique: vers un contrôle
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THE EVOLUTION OF THE REGULATION OF ARTIFICIAL INTELLIGENCE IN MEDICINE: A COMPARATIVE PERSPECTIVE AMONG BRAZIL, EUROPE, AND THE UNITED STATES ¹

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The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
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Abstract

Objective: This study aims to analyze the evolution of the regulation of artificial intelligence (AI) applied to medicine, comparing the regulatory models adopted in the United States and the European Union with those developed in Brazil, and to examine the impacts of these regulatory frameworks on the physician-patient relationship. **Methodology:** The research adopts a qualitative, descriptive, and comparative approach, based on a narrative review of the literature and analysis of primary legal sources, including the European General Data Protection Regulation (GDPR) and the Artificial Intelligence Act (AI Act), the United States' Federal Food, Drug, and Cosmetic Act (FDCA), the 21st Century Cures Act, and FDA guidance documents, as well as Brazil's General Personal Data Protection Law (LGPD) and the Brazilian Artificial Intelligence Strategy (EBIA). The analysis is organized into four thematic sections addressing, respectively, the definition and applications of AI in health, the ethical and legal challenges involved, the international and Brazilian regulatory landscape, and concluding perspectives. **Results:** The findings indicate that the European Union has established the most structured regulatory framework, through a risk-based model under the AI Act that classifies most AI-based medical devices as high-risk, subjecting them to strict transparency, human oversight, and conformity assessment requirements. The United States, in turn, relies on a flexible, iterative regulatory approach centered on the FDA, which distinguishes software functions excluded from the definition of a medical device from those subject to oversight, while facing ongoing challenges related to algorithmic explainability, interoperability, and the adaptation of tort

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**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

liability. Brazil, by contrast, still lacks a specific regulatory framework for AI in health; its normative foundation rests primarily on the LGPD, complemented by soft-law instruments and institutional strategies such as the EBIA, reflecting an incipient but progressively converging regulatory trajectory. Across all three jurisdictions, transparency and algorithmic explainability emerge as central principles for ensuring patient autonomy, accountability, and trust in AI-mediated clinical decision-making.

Keywords: Artificial intelligence; Health law; AI regulation; Medical devices; Algorithmic transparency; Comparative law; Patient autonomy.

Introduction

Artificial intelligence (AI) has established itself as a technology of growing relevance in the field of health, driving transformations in diagnostic, treatment, and clinical management processes. However, the rapid evolution of these tools raises important challenges related to safety, ethics, and legal liability. In this context, the regulation of AI applied to health has received increasing attention from governmental bodies and regulatory entities in different countries, given the need to reconcile the encouragement of technological innovation with patient protection. Moreover, the incorporation of AI into medical practice challenges traditional paradigms of the physician-patient relationship, particularly with regard to trust, communication, autonomy, and human participation in clinical decisions.

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

This article aims to analyze the evolution of AI regulation in the medical field, comparing the regulatory models existing in the United States and Europe with those adopted in Brazil, in addition to examining the impacts of these changes on the relationship between physicians and patients. To this end, Chapter 1 presents the definition of AI, its applications in health, and the main technological developments. Chapter 2 discusses the ethical and legal challenges involved. Chapter 3 discusses the evolution of AI regulation in health, addressing the international landscape, Brazilian regulation, and the main regulatory challenges. Finally, Chapter 4 presents the conclusions and perspectives, highlighting the importance of public policies and regulatory practices that promote an ethical, safe, and humanized application of artificial intelligence in medicine.

It is hoped that this work will contribute to the understanding of the role of public policies in promoting an ethical and safe application of artificial intelligence in medicine, while preserving the humanization of care.

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

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1. Definition and Applications of Artificial Intelligence in Health

Artificial intelligence consists of computational systems capable of performing tasks typical of human intelligence, such as learning, reasoning, and decision-making. In the context of health, AI has been applied on several fronts, from the management of large volumes of data to support for medical decision-making, offering the potential to increase efficiency, reduce errors, and improve patient care. ⁽¹⁾

The concept of Big Data is central to the functioning of artificial intelligence in health, which basically consists of the challenge of managing and analyzing a large volume of data that exceeds conventional processing and storage capacities. The advancement of Big Data has driven significant transformations in the health sector, particularly in research using data mining techniques and in the integration of multiple sources of clinical information, such as medical records, images, and health literature, among others. ⁽²⁾

AI applications can be organized into three main axes: machine learning, which consists of the use of techniques that allow systems to learn from processed data, identifying patterns and making decisions with minimal human intervention, becoming increasingly

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

resilient and adaptive; deep learning, which consists of the use of Artificial Neural Networks (ANNs), mathematically modeling the structure of human neurons — each unit of the ANN performs operations on local data connected by channels with predetermined weights, allowing the intelligent behavior of the network to emerge from the interactions between its processing units; and natural language processing (NLP), which consists of enabling computational systems to understand spoken and written human language, allowing the analysis, recognition, and generation of texts in natural language. ⁽¹⁾

In practice, AI has generated innovative solutions in the health field, having been used to support and accelerate patient screening and diagnosis, analyze imaging exams, predict risk, provide cognitive support, and also facilitate the intelligent search for and retrieval of relevant data, such as biomedical literature. ⁽³⁾

One of the most common applications of artificial intelligence in the medical field is the use of Expert Systems (ES), which “are programs designed to acquire and make available the operational knowledge of a human expert in a given area or field of practice.”

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**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

In medicine, these systems can be used as tools to support diagnosis, prognosis, and therapeutic planning, by analyzing clinical data and presenting information or recommendations to the health professional. However, their results should not replace clinical judgment; it is up to the responsible professional to critically evaluate the information provided and make the final decision regarding patient care. ^(1,2)

In addition, there are Medical Decision Support Systems (MDSS), which are based on decision analysis principles that organize and interpret relevant information about the risks and benefits of different therapeutic alternatives. Their main purpose is to assist physicians and patients in the process of choosing the most appropriate treatment, making decision-making clearer and better founded. ⁽⁴⁾

Even so, patient autonomy remains essential, since it is up to the patient to choose the treatment after due clarification from the responsible professional, who must transparently present the implications and possible risks of each procedure. These systems have been widely used because they provide a structured way of evaluating the various options available, offering technical and analytical support. ⁽⁴⁾

The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States

DOI: <https://doi.org/10.5281/zenodo.23068332>

In general, MDSS can be classified into two groups: those with limited or nonexistent decision-making capacity of their own, aimed at data retrieval, calculation execution, and initial analysis of clinical information; and those equipped with automated reasoning and inference mechanisms, such as expert systems for disease classification or rule-based queries. In their composition, MDSS usually include modules aimed at patient profiling and assessment, diagnosis, and result analysis. ⁽⁴⁾

A notable example is Dr. Watson, developed by IBM, which applies deep learning techniques to identify patterns in large volumes of medical data, providing decision-making support for health professionals. ⁽²⁾

Another point worth highlighting is the evolution of *deep learning* techniques and artificial neural networks, which enable the identification of complex patterns in medical images and clinical data, contributing to the development of tools that support diagnosis and the personalization of care. Inspired by the functioning of biological neural networks, these computational structures can be trained with large datasets and, when subjected to appropriate updating and validation processes, improve their

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

performance when faced with new information and different clinical contexts. ⁽¹⁾

In addition, Natural Language Processing (NLP) has established itself as an essential tool for the interaction between computational systems and health professionals, allowing the automatic analysis of medical texts, electronic health records, and scientific literature. NLP facilitates the extraction of relevant information, reducing the time required for clinical research and contributing to evidence-based decisions. ⁽¹⁾

The impact of AI in the sector also involves organizational and social transformations. The centrality of care, historically based on the physician-patient relationship, is beginning to incorporate technology as a mediator of decisions. This phenomenon may increase efficiency and accuracy, but it also raises challenges regarding patient autonomy, trust in the therapeutic relationship, and the role of the health professional as the final decision-maker. ⁽⁵⁾

Furthermore, technological evolution reinforces the need for integration among clinical knowledge, computational expertise, and ethics. Technology alone does not guarantee positive results; it is essential that its implementation take into account equity,

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

inclusion, and transparency, avoiding biases in the data and ensuring that systems are aligned with the principles of justice and dignity in health care. ^(3,5)

As these technologies become more integrated into everyday clinical practice, the need to reflect on their ethical and legal impacts also grows. The use of intelligent systems in medicine involves decisions that can directly affect the life and integrity of patients, requiring transparency in algorithms, accountability for any failures, and respect for the fundamental principles of bioethics. Thus, understanding the ethical and legal implications of the use of artificial intelligence becomes indispensable to ensure that technological advancement proceeds in harmony with safety and human dignity. ⁽⁵⁾

2. Ethical and Legal Aspects

The application of artificial intelligence in health is not limited to technological advances but involves complex ethical and legal challenges. One of the central principles is equity and inclusion, which should guide the development and implementation of AI systems. Biased tools can undermine public trust, reinforcing existing inequalities in access to health care. For this reason, it is

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

essential that developers carefully assess the quality and representativeness of the data used, identifying possible biases and considering the impacts of the application in different socioeconomic contexts. ⁽³⁾

Although artificial intelligence promotes efficiency, it also presents epistemic problems related to the quality and objectivity of the information produced, since algorithms depend directly on the data and programming decisions of their developers, reflecting values and conceptions about health that may be influenced by economic or cultural interests. This can generate incorrect diagnoses, especially on a large scale, affecting not only individual patients but entire groups and the distribution of resources in health institutions. ⁽⁶⁾

Another critical point concerns normative problems linked to automated decision-making in health care. The use of AI can limit the autonomy of patients and professionals, especially when there is uncritical trust in the supposed objectivity of the decisions offered by the algorithm. At multiple levels — interpersonal, group, institutional, and social — this can lead to the devaluation of the physician-patient relationship, the imposition of unjust decisions,

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

or the transformation of fundamental values regarding what constitutes health care. ^(5,6)

In the legal sphere, transparency emerges as a central ethical principle. AI systems must be intelligible and explainable to health professionals, patients, and regulators, allowing for oversight and public scrutiny.

In the European Union, the General Data Protection Regulation (GDPR) ⁽⁷⁾ establishes duties to inform data subjects about the existence of automated decisions, the logic involved, and their relevance and possible consequences for the data subject. In addition, Article 22 provides for protection against decisions based exclusively on automated processing that produce legal effects or significantly affect the individual, ensuring, in certain cases, guarantees such as human intervention, the expression of the data subject's point of view, and the possibility of contesting the decision. This set of guarantees has been associated with what is known as the right to explanation of automated decisions. ⁽⁸⁾

The regulation of algorithms has become a growing concern in contemporary legal systems, being the subject of debates and formulations in different countries and international organizations. To date, there is a scarcity of binding regulatory instruments, largely

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

limited to legislation aimed at the protection and privacy of personal data. In other areas, the construction of a regulatory framework is still occurring gradually, mainly through soft law instruments, such as codes of conduct, ethical guidelines, and recommendations drawn up by governmental bodies, advisory councils, research centers, and technology companies.⁽⁹⁾

In summary, the ethical and legal aspects of AI in health involve: transparency and explainability, that is, ensuring that algorithms and automated decisions are understandable and auditable; equity and inclusion, aimed at preventing biases in data and applications, promoting justice in access to health care; the autonomy of the patient and the professional, with the objective of ensuring that artificial intelligence complements, rather than replaces, human judgment; responsibility and traceability, since it is necessary to clearly define the actors responsible for automated decisions, avoiding unjust or disproportionate harm; and harmonization with human rights and legislation, so as to integrate the protection of personal data.^(5,6)

In light of these ethical and legal challenges, it is clear that the regulation of artificial intelligence in health needs to evolve to keep pace with technological advancement, ensuring that its use

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

respects fundamental rights and human dignity. The need for clear regulatory structures and solid ethical principles reinforces the importance of considering different international experiences and practices, which can serve as a reference in the construction of effective and safe policies.

3. Evolution of AI Regulation in Health

3.1 International Landscape

The development and application of artificial intelligence in health has drawn increasing attention in international legal systems, given the complexity and the ethical and social risks involved. In recent years, different countries and international organizations have sought to create regulatory instruments to govern the use of AI, focusing on privacy, safety, transparency, and the protection of human rights.⁽⁹⁾

One of the main reference models is the European Union's General Data Protection Regulation (GDPR)⁽⁷⁾, in force since May 2018. This regulation, in addition to protecting personal data, established the so-called right to explanation, ensuring that individuals affected by automated decisions can understand the criteria used and contest such decisions.⁽⁸⁾

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

The GDPR provides for human intervention and the opportunity to review decisions, consolidating what is known as algorithmic due process. European regulation is often cited as a global benchmark, inspiring policies and legislation in other countries, particularly with regard to transparency and accountability in the use of AI in health. ⁽⁷⁾

In addition to the GDPR, several international initiatives seek to develop ethical and technical guidelines for AI in health. Organizations such as the OECD, UNESCO, and the World Health Organization (WHO) have published recommendations on the safe, transparent, and responsible use of AI technologies. Although not binding, such guidelines offer parameters in this regard. ^(9,10)

Another important European regulatory milestone is Regulation (EU) 2024/1689, known as the Artificial Intelligence Regulation or AI Act ⁽¹¹⁾, which establishes harmonized rules for the development, placing on the market, and use of artificial intelligence systems in the European Union. The regulation adopts a risk-based approach, imposing distinct obligations according to the purpose, the context of use, and the potential impact of the system on health, safety, and fundamental rights. ⁽¹⁰⁾

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

In the field of medicine, the classification of an AI system as high-risk depends on the specific characteristics of its use. Under Article 6 of the *AI Act*, systems that constitute safety components of medical devices, or that are themselves medical devices, will be considered high-risk when the product is subject to third-party conformity assessment under applicable European legislation. Thus, not every AI tool used in the health field is automatically classified as high-risk; rather, an analysis of its intended purpose, function, and the regulatory regime to which it is subject is required. ^(10,11)

The final regulation establishes that classification depends on specific criteria, including whether the product is subject to third-party conformity assessment, and not merely on the fact that the technology is used in health care. The *AI Act* entered into force on August 1, 2024, and its provisions follow a gradual timetable of application. ⁽¹¹⁾

The European Regulation classifies risks into four categories:

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

Risk Level	Legal Basis	What it is	Obligations
Unacceptable Risk	Art. 5	AI practices prohibited for violating fundamental EU values	Total ban: may not be placed on the market, put into service, or used in the EU
High Risk	Arts. 6–49 + Annex III	Systems that may cause significant harm to health, safety, or fundamental rights	Mandatory requirements: risk management system, quality of training data, technical documentation, event logging, transparency to users, human oversight, accuracy/robustness/cybersecurity, conformity assessment prior to marketing
Limited Risk	Art. 50	Systems with specific transparency risks (do not cause serious	Transparency obligation: inform the person that they are interacting with an AI, or that the content was generated/manipulated by AI

The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative Perspective Among Brazil, Europe, and the United States DOI: https://doi.org/10.5281/zenodo.23068332			
		harm, but may deceive)	
Minimal Risk	—	The vast majority of AI systems, with no relevant risk identified	No specific legal obligations: free use, with voluntary adherence to encouraged codes of conduct
Author's own elaboration, based on European Regulation 2024/1689 Considering the criteria established by the AI Act, AI-based medical support devices predominantly fall into the high-risk category, which imposes stricter requirements and obligations on developers and providers. ⁽¹⁰⁾ The purpose of the AI Regulation is to ensure that systems placed on the market are safe and comply with current legislation on fundamental rights and Union values. The high-risk classification in medicine is specifically aimed at mitigating potential biases, errors, and the lack of transparency that may arise in the clinical context. ⁽¹⁰⁾ In the United States, the Food and Drug Administration (FDA) has been driving a flexible regulatory model, focused on ensuring			
			64

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

the safety of AI-based devices, with an emphasis on iterative processes and continuous machine learning. ⁽³⁾

The regulation of AI in medicine in the United States is complex, multifaceted, and continuously evolving, involving federal laws, specific health regulations, and state tort liability laws. The central regulatory agency for the oversight of clinical AI systems is the Food and Drug Administration (FDA), which operates under the Federal Food, Drug, and Cosmetic Act (FDCA) ⁽¹²⁾. The FDCA regulates the safety and efficacy of drugs and medical devices, which includes certain clinical artificial intelligence software. ⁽³⁾

According to the FDCA's definition (21 USC § 321(h)(1)) ⁽¹²⁾, a medical device is

an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, that is: recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them; intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in humans or other animals; or intended to affect the structure or any function of the body of humans or other animals; and which does not achieve its primary intended purposes through chemical action within or on the body of humans or other animals,

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

In 2016, the 21st Century Cures Act ⁽¹³⁾ amended this definition by introducing Section 520(o), which excludes certain computer program (software) functions from the medical device category, recognizing that not every health-oriented program should be subject to the same regulatory oversight, provided they are intended to display, analyze, or print medical information about a patient or other medical information (such as peer-reviewed clinical studies and clinical practice guidelines); to support or provide recommendations to a health professional regarding the prevention, diagnosis, or treatment of a disease or condition; and to allow the health professional to independently review the basis for the recommendations presented by the software, such that it is not intended for the professional to rely primarily on those recommendations to make a clinical diagnosis or treatment decision for an individual patient. ^(13, 14)

In the case of clinical decision support systems, the exclusion applies only when the legal criteria are cumulatively met. The software's function may not be intended to acquire, process, or analyze medical images, signals from in vitro diagnostic devices, or

The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative Perspective Among Brazil, Europe, and the United States

DOI: <https://doi.org/10.5281/zenodo.23068332>

patterns from signal acquisition systems. In addition, it must be intended to display, analyze, or present medical information; to support or provide recommendations to a health professional regarding prevention, diagnosis, or treatment; and to allow that professional to independently examine the basis for the recommendation, such that it does not predominantly depend on it to formulate a diagnosis or make an individual therapeutic decision.⁽¹⁴⁾

The FDA classifies medical devices into three categories: Class I, considered low risk to users; Class II, moderate risk; and Class III, considered high risk to users.^(12,14)

This understanding was detailed in the document “Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD)”⁽¹⁵⁾, published by the FDA in 2019, which outlines the guiding principles for the oversight of these systems.⁽¹⁴⁾

This approach was later developed through more specific documents and guidance. In the current final guidance on Predetermined Change Control Plans (PCCPs)⁽¹⁶⁾, published in August 2025, the FDA recommends that the manufacturer describe

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

in advance the planned modifications to the device, the methodology to be used to develop, validate, and implement such changes, and the assessment of their possible impacts. When the PCCP is reviewed and authorized as part of a regulatory submission under the 510(k), *De Novo*, or PMA procedures, the modifications covered by the plan may be implemented without a new individual submission, provided they remain within the authorized limits and the safety and efficacy of the device are preserved (FDA, 2025). The guidance document further clarifies that these guidelines constitute non-binding recommendations, reflecting the agency's current understanding of the subject. This approach demonstrates the U.S. regulatory effort to balance technological innovation and safety, while at the same time posing the challenge of keeping pace with the rapid evolution of machine learning algorithms and their ethical and legal implications for health care. ⁽¹⁶⁾

The U.S. regulatory approach also considers the product's total life cycle, encompassing development, validation, transparency, bias prevention, performance monitoring, and post-market update management. With regard to clinical decision support systems, FDA guidance seeks to differentiate software functions excluded from the legal definition of a medical device from those that remain

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

subject to regulatory oversight, particularly according to the health professional's ability to independently review the basis for the recommendations presented by the system. ^(3,16)

A relevant challenge is the explainability of AI tools, since many deep learning-based systems function as “black boxes,” making it difficult to ensure transparency in the decision-making criteria. U.S. regulators consider that a lack of explanation may compromise trust, accountability, and post-market monitoring of these technologies. ^(3,14)

Another challenge faced by the United States is the interoperability of health systems. The integration of artificial intelligence software with different clinical platforms and databases requires uniform technical and regulatory standards capable of ensuring secure and effective communication between systems. The FDA collaborates with other institutions, such as the Federal Trade Commission (FTC) and the National Institute of Standards and Technology (NIST), in formulating technical standards and best practices for the ethical and safe use of algorithms. ^(3,13,15)

The privacy of patient data and the representativeness of the datasets used to train AI systems are other important obstacles.

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

HIPAA provides a minimum floor of protection for health information in the United States, but its scope is limited. This creates regulatory gaps, especially when data comes from non-traditional sources or sources not covered by HIPAA. ⁽¹⁴⁾

It should also be noted that tort liability in U.S. states is still not fully adapted to AI technologies in health care. The intersection between FDA regulatory approval and state liability actions creates uncertainty as to who should be held accountable when AI systems cause harm. There are tensions between federal oversight and state litigation. ^(3, 14)

In summary, in the United States, the regulation of AI in health presents a significant regulatory framework centered on safety, efficacy, privacy, and accountability, but faces challenges such as the rapid evolution of technology, the need for algorithmic transparency, the use of large-scale data, and the adaptation of the tort liability system. Current regulatory practices are important but still require improvement to keep pace with innovation in the sector.

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

3.2 Brazilian Regulation

Although less advanced, Brazil has begun discussions on guidelines for the responsible use of AI in health, aligning itself with international recommendations and seeking to promote safe and transparent access, particularly in digital health public policies. This movement was driven by national science and technology policies, such as Ordinance No. 1,122, of March 19, 2020 ⁽¹⁷⁾, issued by the then Ministry of Science, Technology, Innovations, and Communications (MCTIC), which included artificial intelligence among the “Enabling Technologies” prioritized for the country's scientific and technological development for the 2020–2023 period. This recognition reinforced the importance of AI as a strategic tool for innovation and for the improvement of public services, including the health sector.

At the national level, the Brazilian Artificial Intelligence Strategy (EBIA) ⁽¹⁸⁾, established by the Ministry of Science, Technology, and Innovations (MCTI) in 2021, represents an important milestone in this debate. The EBIA is structured around thematic axes, the first of which is legislation, regulation, and ethical use, of a cross-cutting nature. This axis recognizes the need to balance the protection and safeguarding of individual rights, the

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

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creation of structures that encourage technological development, and the establishment of legal parameters capable of providing legal certainty to the various actors involved in the value chain of autonomous systems.

This approach seeks to promote responsible innovation without disregarding the potential ethical, social, and legal risks inherent in the use of AI in health.

The landscape of technology adoption also reveals relevant aspects, since Brazil stands out in relation to Europe with regard to the number of companies that use AI for workflow automation, followed by applications in image recognition and processing, a trend that is particularly significant for the health sector, where diagnoses based on medical images are increasingly common. In other types of use, the differences between Brazilian and European companies are small, although in Europe there is a more homogeneous distribution among the different types of applications, indicating a more balanced technological maturity.⁽¹⁹⁾

In the legal field, the regulation of artificial intelligence in health is closely linked to the General Personal Data Protection Law (LGPD — Law No. 13,709/2018)⁽²⁰⁾, enacted in August 2018 and in force since September 2020, with administrative sanctions

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

applicable as of August 2021. Although the LGPD does not explicitly mention “artificial intelligence” or “algorithm,” the law establishes principles and rights that directly impact the application of AI in health, such as transparency, the explanation of automated decisions, and the possibility of reviewing such decisions. ⁽⁹⁾

These foundations are compatible with international ethical and regulatory principles and constitute the basis for future AI regulation in the country, particularly in the field of health, where the handling of sensitive data requires a high level of security and accountability. ⁽⁶⁾

In addition, the protection of trade and industrial secrets must be weighed together with the right to explanation. Brazilian legislation provides for audits in cases of suspected discrimination, balancing business interests and individual rights, reinforcing the need for harmonization between technological innovation and human rights. ⁽⁹⁾

Article 20 of the LGPD ⁽²⁰⁾ guarantees data subjects the right to request the review of decisions made solely on the basis of automated processing of personal data that affect their interests. Unlike the European GDPR, Brazilian law does not provide for a mandatory obligation of automatic human intervention, nor the

The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative Perspective Among Brazil, Europe, and the United States

DOI: <https://doi.org/10.5281/zenodo.23068332>

right not to be subject to exclusively automated decisions. The original wording provided for the review to be carried out by a “natural person,” but this provision was amended by a provisional measure and subsequently consolidated into law, allowing future regulations to define the need for human oversight. ⁽⁹⁾

This legislative openness creates room for policies such as the EBIA and infra-legal regulations to establish additional requirements for explainability and auditing in critical applications, such as those in health care. ^(9,18)

Although the LGPD focuses primarily on the protection of personal data, it has important implications for AI in health, especially with regard to algorithmic transparency. The law ensures that anyone affected by automated decisions has access to clear information about the criteria and procedures used, promoting intelligible explanations and enabling the contestation of results. This mechanism is connected to the ethical principle of transparency, considered fundamental in the use of AI in health contexts, since it allows patients, professionals, and regulators to understand how the systems actually work. ^(9,20)

This guideline is consistent with the EBIA's emphasis on the responsible governance of AI systems, which includes mechanisms

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

for accountability, monitoring, and continuous auditing of algorithms used in sensitive sectors. ^(6,18)

Beyond the LGPD, Brazil is still at an early stage in the development of specific regulations for artificial intelligence in health. The current approach combines soft law — through codes of conduct, professional council guidelines, recommendations from public bodies, and regulations from research institutes — with the systematic interpretation of the LGPD, the Federal Constitution, and the Consumer Protection Code. These measures aim to balance the right to explanation and review with the protection of trade and industrial secrets, which are essential for the development of AI-based business models. ^(6,9)

Brazilian regulation also seeks to prevent discrimination and injustice arising from automated decisions. Studies indicate that the growing inclusion of AI in clinical and administrative decisions can generate normative and epistemic problems, affecting patient autonomy, the physician-patient relationship, and the distribution of health resources. ^(5,6)

For this reason, the legislation emphasizes the need for audits and review mechanisms, especially in cases of suspected discrimination or harm to fundamental rights. ^(9,18,20)

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

This concern reflects a movement toward alignment with international AI governance practices, although Brazil still lacks robust regulatory instruments detailing specific obligations for the health sector. ⁽⁶⁾

In summary, although Brazil does not yet have a specific regulatory framework for AI in health, the LGPD establishes important foundations that guide the ethical, transparent, and responsible use of these technologies. The development of infra-legal regulations and future specific standards will be essential to consolidate rights such as explainability, review of automated decisions, traceability, and accountability, aligning the use of AI with ethical principles and human rights. ^(6,9)

The inclusion of AI among the strategic priorities for science and technology (Ordinance No. 1,122/2020) and the creation of the EBIA (Ordinance No. 4,617/2021) represent significant institutional milestones in this process. Both reinforce the Brazilian State's intention to develop an ecosystem of responsible innovation, balancing the encouragement of research with the protection of rights. This trajectory shows that the country has been building a regulatory path that, although still incipient, seeks to converge with

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

international regulatory benchmarks and strengthen legal certainty in the use of AI in health. ^(17,18)

4. Conclusion

The regulation of artificial intelligence (AI) in health is an essential and emerging topic worldwide, facing the challenge of keeping pace with algorithms that, unlike traditional medical devices, are in constant change and learning. This technical complexity requires a delicate balance between encouraging technological innovation and ensuring that the use of these tools invariably results in benefits for human beings, respecting safety and fundamental rights. ^(9,10)

In Brazil, the initial milestone of this debate is the General Personal Data Protection Law (LGPD — Law No. 13,709/2018), which, although it does not explicitly mention “AI,” establishes principles of transparency and the right to explanation and review of automated decisions. ⁽⁹⁾ Article 20 of the LGPD guarantees data subjects the right to request the review of decisions made solely on the basis of automated processing of data that affect their interests. In addition, the Brazilian Artificial Intelligence Strategy (EBIA), established in 2021, is structured around axes such as “legislation,

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

regulation, and ethical use,” seeking to balance the safeguarding of individual rights with the creation of legal parameters that provide legal certainty. In addition, MCTIC Ordinance No. 1,122/2020 included AI among the priority “Enabling Technologies” for the country's strategic development. ^(17,18)

Internationally, the European Union established a global benchmark with the Artificial Intelligence Regulation (AI Act), which adopts an approach based on four risk levels ⁽¹⁰⁾: minimal, limited, high, and unacceptable. AI systems intended for medical diagnosis are classified as high-risk, requiring strict compliance with ethical and safety standards given their potential impact on human life. ⁽¹⁰⁾

In the United States, central oversight rests with the FDA, which operates under the Federal Food, Drug, and Cosmetic Act (FDCA) to ensure the safety and efficacy of clinical software. The 21st Century Cures Act of 2016 detailed criteria for certain clinical decision support software to be excluded from the definition of a medical device, provided it allows the health professional to independently review the basis for the recommendations presented. More recently, the FDA's August 2025 guidance on Predetermined Change Control Plans (PCCPs) allowed manufacturers to implement

**The Evolution of the Regulation of Artificial Intelligence in Medicine: A Comparative
Perspective Among Brazil, Europe, and the United States**

DOI: <https://doi.org/10.5281/zenodo.23068332>

planned iterative modifications without the need for new individual submissions, provided that safety and efficacy are preserved. ^(14,16)

In summary, the safe advancement of AI in health depends on building a robust ethical and regulatory framework that ensures algorithmic explainability and transparency. Transparency is regarded as the key principle indispensable for other rights, such as patient autonomy and civil liability, to be effectively realized. The consolidation of responsible governance practices and the continuous monitoring of the product life cycle will be crucial for technology to effectively contribute to health, strengthening the trust of professionals and patients in the care system.

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— Luiz Sales do Nascimento

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EUROPEAN INTEGRATION AS A MODEL OF POLITICAL AND ECONOMIC DEVELOPMENT ORIENTED TOWARDS GLOBALIZATION ¹

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European integration as a model of political and economic development
oriented towards globalization

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Abstract

After briefly presenting the historical formation of the European Union, this study sets out to identify the aspects that render its composition — the outcome of a historical process aimed at integrating the European nations into a single economic and political bloc — a positive paradigm of international development, an inspirational model worthy of replication by other groupings of States, particularly in view of both the positive results achieved and the need to optimize responses to

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the challenges inherent in today's globalized world, in a peaceful and cooperative manner. The subject gains added significance insofar as the growing prominence of international global governance presents itself as an irreversible trend, together with a resignification of the concept of state sovereignty. Accordingly, notwithstanding its evident vicissitudes, this model demonstrates the political feasibility of its implementation, always taking into account the particular characteristics of each prospective grouping, geography, ideology, culture, and other factors not precluding a collaborative union, capable of resulting in political, social, and economic integration such as to foster, along the lines of the European reference, the long-sought development of all national States committed to such unification. This work follows an exploratory, descriptive research design grounded in bibliographic material, namely, printed books and scientific articles retrieved from the Scielo, Google Scholar, and ScienceDirect databases, obtained through searches using the same keywords set out below, together with other authoritative references on the subject, as indicated at the end.

Keywords: European Union; political integration; economic integration; global governance; globalization.

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Introduction

Arising from a gradual historical construction undertaken to meet economic and political needs, the European Union, the product of the joint endeavor and shared efforts of 27 sovereign nations pursuing communion and the conjugation of interests, unveils a new paradigm of political composition with clear legal, economic, social, and cultural repercussions, one that responds to the recent and irreversible phenomenon of globalization.

Contributing to this phenomenon is the fact that we are living within the flow of a postmodern information society, in which the material and territorial limits of a geographical nature no longer present themselves as obstacles to real-time interaction. The adaptation of human relations to a globalized outlook, grounded in criteria of cooperation and non-belligerent negotiation among States, denotes a productive political maturation that, in light of the evidence, undoubtedly generates progress and development.

In this sense, as a pioneer of this utilitarian and visionary conception, the European Union emerges as a new and successful model of communal formation which, notwithstanding the idiosyncrasies that render it unique and therefore incomparable, carries within itself principles, attributes, and purposes that indeed

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

serve as a kind of inspirational prototype, capable of adoption by other blocs of nations that find, in a similarly structured composition, an integrative mechanism and a driver of development.

In order to bring this perspective to light, the first chapter offers a historical overview of the formation of the European Union, tracing the gradual process of political and economic construction that led to its present configuration.

In the second chapter, following a brief examination of the conception of sovereignty arising from the Peace of Westphalia, and in light of the phenomenon of globalization, consideration will be given to the new outlook that must be applied to global problems and challenges, given the diffuse and cross-border character they have assumed, together with the need to relativize sovereignty as one of the mechanisms of integration indispensable to the new European composition. This chapter will also address the positive aspects of European communal formation, based on the analysis of three indicators used solely for illustrative purposes to exemplify the success of this economic-political aggregate: the increase in GDP and the decline in the unemployment rate over the

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

past 12 years, and the growing commercial relevance assumed within the global scenario.

Finally, the concluding remarks will point to how the success of the European Union's formation, as it presents itself today, the result of a highly well-engineered process of political articulation, establishes a new inspirational model of political and economic integration of common interests among Nation-States, one that may be replicated ambitiously and feasibly by other regional blocs around the world, chiefly owing to its virtue of fostering development through its intrinsic vocation for reconciling the dilemmas, purposes, aspirations, and human needs of its members with a virtually cross-border and globalized world.

1. The historical trajectory of the formation of the European Union

With the end of the Second World War on 8 May 1945, the European countries involved in the conflict emerged with their economies shattered, having suffered strikingly extensive damage and a death toll even greater than that of the First World War, leaving the entire continent and its principal nations weakened.

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

Conversely, the United States became the richest and most powerful nation in the world; during the conflict, it had tripled its industrial capacity, becoming a genuine global economic power, though concerned with the growth of socialism which, with the former USSR as its greatest exponent, represented a potential threat to capitalism.

With a view to erecting a political and economic barrier in Western Europe to contain the advance of the Soviet 'threat,' on 5 June 1947 George C. Marshall, United States Secretary of State, announced the so-called Marshall Plan, which was implemented between 1948 and 1951 under the Truman administration.

The Marshall Plan, subsidized by the American government and coordinated by the Organisation for European Economic Co-operation (OEEC)⁵, consisted of a financial contribution made available by the United States to Europe, represented by the injection of approximately 17 billion dollars into the European economy through the granting of low-interest loans and cash grants

⁵Created on 16 April 1948 and headed by Robert Marjolin of France, its purpose was to help administer the Marshall Plan. As of 1961, the 'Organisation for European Economic Co-operation' (OEEC) was renamed the 'Organisation for Economic Co-operation and Development' (OECD), admitting non-European countries and assuming a broader, multisectoral, and intercontinental scope of action.

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

subject to certain conditions, for the benefit of countries damaged by the war (BRASIL, 2026; OECD, 2026; PORTO, 2019).

As intended, the European nations recovered, and the ties between the United States and Europe grew closer.

Meanwhile, Winston Churchill, who advocated the creation of the 'United States of Europe,' referring to his fellow citizens as the European family, brought a number of recommendations to this effect before the Hague Congress, such as the creation of a deliberative European Assembly (European Parliament), a special European Council entrusted with preparing political and economic integration, and the establishment of a European Court of Justice (SILVA, 2001; EUROPEAN UNION, 2026a; CVCE.EU, 1948).

1949 saw the creation of NATO and the Council of Europe (NATO, 2026).

Still aiming at postwar reconstruction, on 9 May 1950 — a date now designated 'Europe Day' — Robert Schuman, French Minister of Foreign Affairs, in partnership with Jean Monnet, presented a plan for the implementation of cooperative measures among European countries willing to promote the integration of Western Europe's coal and steel industries.

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

Thus, on 18 April 1951, on the basis of what came to be known as the Schuman Plan, Germany, France, Italy, the Netherlands, Belgium, and Luxembourg jointly signed the Treaty of Paris, establishing the European Coal and Steel Community (ECSC)⁶, placing their heavy coal and steel industries, the driving forces of the economy of the time, under a common management system, facilitating movement between producing areas and consuming regions, and removing tax barriers (FERNANDES; FREIRE E ALMEIDA, 2021; EUROPEAN UNION, 2026b; EUROPEAN UNION, 2026c).

This was because, while coal was essential as the energy source needed to drive Europe forward, steel would lay the foundations of reconstruction, indispensable in every corner of Europe.

On 25 March 1957, the two Treaties of Rome established the European Economic Community (EEC) and the European Atomic Energy Community (EAEC, or Euratom) (EUROPEAN UNION, 2026d).

The rise of Community legislative activity came with the first session of the European Parliament on 19 March 1958, at which Schuman was elected its president.

⁶This Community formally began operating on 23 July 1952.

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

The creation of EFTA (the European Free Trade Association) on 3 May 1960, and the establishment of a free-trade area on that same date, conferred greater freedom of movement on trade in goods among the European countries, “while nonetheless allowing each member to pursue its own commercial policy with regard to foreign trade” (PORTO, 2017; EFTA.INT, 2026); visible barriers were eliminated (FERNANDES; FREIRE E ALMEIDA, 2021).

This was followed by the adoption of the Common Agricultural Policy (CAP), implemented on 30 July 1962, which sought to give the countries of the European Economic Community control over food production, once again grounded in integrative and potentially development-oriented purposes (EUROPEAN COMMISSION, 2026).

Next, as a further step toward unity and integration, the three Communities established up to that point, the European Coal and Steel Community (ECSC), the European Economic Community (EEC), and the European Atomic Energy Community (Euratom), merged on 8 April 1965 under the name 'European Communities,' likewise adopting a single administrative body and a single Council, and establishing the common external tariff known as the CET, all pursuant to the pact concluded under the Merger Treaty, or Treaty of Brussels (EUR-LEX, 2026a; EUR-LEX, 2026b).

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

The elimination of customs duties among member countries as of 1 July 1968 became a reality, promoting the free movement of goods produced among them through a common commercial policy, by applying a single external tariff and by negotiating contracts with third countries jointly (EUROPEAN UNION, 2026d).

On 1 January 1973, the Kingdom of Denmark, Ireland, and the United Kingdom of Great Britain and Northern Ireland formally acceded to the European Communities; Greece (the Hellenic Republic) followed in 1981, and Spain and Portugal five years later, on 1 January 1986.

In 1986 the Single European Act (SEA) was also signed which, by amending the Treaties of Rome, sought to eliminate, within a six-year period, the barriers to the free flow of trade within the European Union, establishing the so-called 'Single Market' (EUR-LEX, 2026c), extending the rupture already begun with the customs union by also removing the “invisible barriers (non-tariff barriers, NTBs)” (PORTO, 2017, p. 195), thereby providing for the free movement of goods, services, and factors — namely, labor and capital.

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

Finally, on 7 February 1992, with the signing of the Maastricht Treaty in the Netherlands, the European Union was born, although it entered into force only on 1 November 1993 (EUR-LEX, 2026d).

Fig. 1. The Treaty on European Union, also known as the Maastricht Treaty, surrounded by the signatures of the 12 Ministers of Foreign Affairs and Finance of the Member States



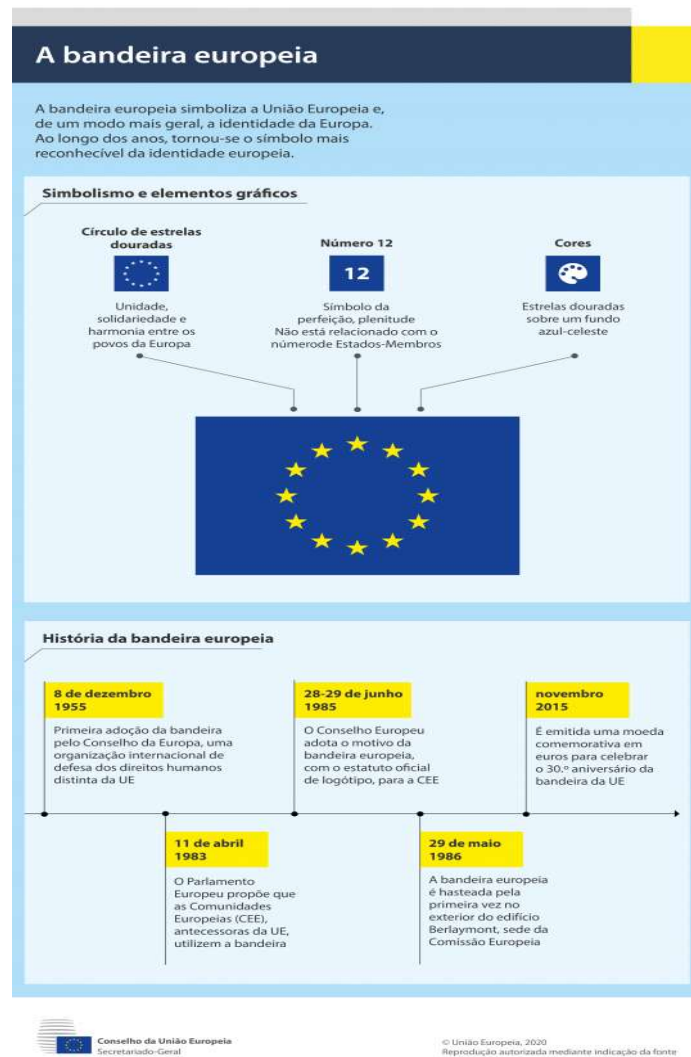
(Source: <https://www.europarl.europa.eu/about-parliament/pt/in-the-past/the-parliament-and-the-treaties/maastricht-treaty>).

The following is the representative flag, the political symbol of the Community's identity, whose history and explanatory details are shown in Figure 2 below:

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

Fig. 2. The European flag



(Source: https://european-union.europa.eu/principles-countries-history/symbols/european-flag_pt).

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

On 1 January 1993, the Single Market also finally came into force, promoting the opening and free movement of persons, goods, services (some not fully liberalized), and capital.

The European Economic Area (EEA) came into being on 1 January 1994, joining the EU Member States with the three EEA-EFTA States (Iceland, Liechtenstein, and Norway) in an Internal Market governed by the same basic rules, enabling goods, services, capital, and persons to move freely throughout the EEA in an open and competitive environment — a concept known as the four freedoms (EFTA.INT, 2026)⁷.

The European Union gained three new members on 1 January 1995: Austria, Finland, and Sweden.

That same year, on 26 March, the Schengen framework began to apply: Belgium, France, Germany, Luxembourg, the Netherlands, Portugal, and Spain, by signing what is regarded as the European Union's greatest achievement (first the Schengen Agreement, on 14 June 1985, and subsequently the Schengen Convention, on 19 June

⁷Persons, goods, services, and capital currently circulate freely among the 30 EEA countries (the EU-27 plus Iceland, Liechtenstein, and Norway). Switzerland does not participate in the EEA but has access to the single market. Available at: https://european-union.europa.eu/principles-countries-history/history-eu/1990-99_pt. Accessed on: 14 Mar. 2026.

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

1990) agreed upon the free movement of both Community and non-Community travelers among these countries in a secure manner and without passport controls at the borders (EUR-LEX, 2026d).

On 1 May 2004, ten new countries joined the EU: Cyprus and Malta, together with eight countries of Central and Eastern Europe, the Czech Republic, Estonia, Hungary, Latvia, Lithuania, Poland, Slovakia, and Slovenia, finally putting an end to the post-Second World War division of Europe.

Romania and Bulgaria joined the bloc on 1 January 2007, and Croatia on 1 July 2013, bringing the total at that time to 28 nations (FERNANDES; FREIRE E ALMEIDA, 2021).

Subsequently, a referendum held on 23 June 2016 expressed the will of 52% of voters in the United Kingdom to leave the European Union after more than 40 years of membership⁸ (GOV.UK, 2026; EUROPEAN COMMISSION, 2026b).

⁸This withdrawal, known as Brexit, took place on 31 December 2020 and was consolidated on 1 January 2021, once again reducing the European Union to a composition of 27 countries (FERNANDES; FREIRE E ALMEIDA, 2021).

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

In 2021, twenty-six countries⁹ formed part of the passport-free Schengen area, including Iceland, Liechtenstein, Norway, and Switzerland (countries that are not members of the European Union) (PORTUGUESE CONSULATE GENERAL IN SÃO PAULO, 2026).

On 1 January 2023, Croatia became the newest Member State to join the Schengen area, bringing the total number of participating countries to 27.

More recently, Romania and Bulgaria completed their accession to the Schengen area in two stages: checks at internal air and maritime borders were lifted on 31 March 2024, and checks at internal land borders were removed on 1 January 2025, bringing the Schengen area to a total of 29 countries — 25 of the 27 European Union Member States, together with Iceland, Liechtenstein, Norway, and Switzerland. Cyprus remains, at present, the only European Union Member State not yet fully integrated into the Schengen area (COUNCIL OF THE EUROPEAN UNION, 2026a; EUROPEAN COMMISSION, 2026g).

⁹These are: Germany, Austria, Belgium, Denmark, Slovakia, Slovenia, Spain, Estonia, Finland, France, Greece, Hungary, Iceland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, Norway, the Netherlands, Poland, Portugal, the Czech Republic, Sweden, Switzerland.

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

The euro was established as scriptural currency, limited to commercial and financial transactions, on 1 January 1999, and was introduced in that capacity in only eleven countries, designated the 'eurozone': Germany, Austria, Belgium, Spain, Finland, France, Ireland, Italy, Luxembourg, the Netherlands, and Portugal.

Physical currency was introduced only in January 2002 (FERNANDES; FREIRE E ALMEIDA, 2021). Since then, the eurozone has continued to expand: Croatia adopted the euro on 1 January 2023, becoming its twentieth member, and Bulgaria followed on 1 January 2026, becoming its twenty-first member (EUROPEAN CENTRAL BANK, 2026; COUNCIL OF THE EUROPEAN UNION, 2026b).

As of the time of writing, the following twenty-one Member States have adopted the euro as their official currency: Austria, Belgium, Bulgaria, Croatia, Cyprus, Estonia, Finland, France, Germany, Greece, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Portugal, Slovakia, and Slovenia, with Czechia, Denmark, Hungary, Poland, Romania, and Sweden remaining outside the eurozone (EUROPEAN CENTRAL BANK, 2026).

With the final monetary integration (technically termed positive integration) made possible by the single currency, the most

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

sophisticated and singular form of political-economic integration in world history was consolidated (PORTO, 2019).

2. Revisiting the peace of Westphalia and the relativization of the concept of sovereignty as a mechanism for managing integration in the formation of the European Union

Crises provoke ruptures and the destabilization of a given state of affairs, which at times assumes a positive character owing to the productive transformation it ultimately brings about.

A classic example of this assertion is the Thirty Years' War, a bloody and inglorious event in human history which, followed by the well-known 'Peace of Westphalia' of 1648, enabled States to coexist respectfully and peacefully through the design and experience of the concept of state sovereignty, already developing in embryonic form since the fifteenth century (FERNÁNDEZ; GONZÁLEZ, 2018).

Through the eventual consolidation of this new order, the world sought a political structure of power based on peace and mutual respect, woven together through concordant interaction among national States, abandoning the conflictual conception

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

theretofore prevailing and apparently inseparable from the very notion of power.

Adopted and implemented worldwide, both in domestic policy and in international relations, the concept of sovereignty arising from the Peace of Westphalia is still invoked as a constitutive element of the State, retaining as its foundational premise the bases of its original conception — regarding as a nation any entity endowed with sovereign power: one, absolute, and indivisible.

“Pero es en Westfalia donde la soberanía recibe un reconocimiento internacional y donde se limita el modo a ser ejercida en los siglos posteriores. La pluralidad de Estados negociadores y su intención de representar a la voluntad soberana deriva en un concepto modificado de soberanía. Este concepto mantiene su valor absoluto y total al interior de las fronteras, pero en lo exterior se ve limitado por otras soberanías, y luego por las normas de Derecho Internacional.” (FERNÁNDEZ; GONZÁLEZ, 2018)¹⁰

¹⁰ Free translation: “It is at Westphalia, however, that sovereignty receives international recognition, together with the manner in which it would be exercised in the centuries that followed. The plurality of negotiating States and their intention to represent the sovereign will gave rise to a modified concept of sovereignty. This concept retains its absolute and total character within borders, but abroad it is limited by other sovereignties and, subsequently, by the rules of international law.”

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

That is, internally, as a synonym for supremacy among the derivative legal norms themselves, an exclusive and excluding power from which functions and authority are assigned with a view to achieving national objectives, and externally, as a synonym for independence and legal equality grounded in an originality that distinguishes each State from the other derivative internal orders, projecting itself onto the international system as the sole interlocutor.

Over time, however, with human reorganizations and, once again, the onset of crises destabilizing the concepts and foundations theretofore in place, a reconfiguration of the concept of sovereignty became necessary (FERNÁNDEZ; GONZÁLEZ, 2018).

Although not abandoned or diminished, it is said today that there is a clear relativization in the perception of sovereignty, arising from the process of globalization — notably since the two World Wars of the twentieth century which, as seen in the previous chapter, intensified by the post-Cold War period of the 1990s, served as the driving force behind a new European political construction that began incipiently with the Marshall Plan.

This configuration of a 'new global order,' as termed by Castells, emerging from the power of global networks, social

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

movements, and the unrelenting advance of technology, although it finds insurgent critics¹¹, is a political and social reality that must necessarily be confronted (CASTELLS, 2018).

The ability of States to navigate these internationally oriented phenomena on their own is challenged not only by the interdependence of the economy and of financial and monetary markets worldwide, but also by the inherently cross-border nature of environmental problems, by the boundlessness and lack of control over communication imposed by technology and artificial intelligence, and by the manner in which virtually all human demands have taken on a trans-international character, as exemplified by the globalization of the media and of electronic communication, of crime, of social protest, and of rebellion in the form of terrorism, all of which “compromise the autonomy and decision-making capacity of the Nation-State” (CASTELLS, 2018; NASSER, 2021).

It is certain, therefore, that a “new system of power” has emerged, characterized “by the plurality of sources of authority

¹¹ Among the criticisms leveled is the prognosis that, from a philosophical standpoint, globalization represents the arrival of the 'Big Brother' foreseen for 1984 in the classic work of the same name by George Orwell (Castells, 2018).

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

(and, one might add, of power), with the Nation-State being merely one of those sources” (CASTELLS, 2018).

Consequently, the unification of these same Nation-States into like-minded blocs, for the sake of dynamic and efficient action, presents itself as a trend inherent to the very multifaceted and internationalized set of issues to be addressed, which for the same reason demand a response of comparable scope, in light of globalization.

And starting from the premise that what is global is unified, Schuman's perspective in planting the seed of European integration proves visionary.

Obviously, throughout this entire process, as previously analyzed, an extensive political engineering effort was required, negotiated on the basis of reciprocal concessions in order to accommodate interests cooperatively, in a sequence of relaxations and adjustments of rules and conduct aimed at an integrated composition of nations.

On the basis of these premises, a reflection is already emerging on the role that sovereignty is to play elsewhere within this new political design, given that the admission of norms external to the Nation-State — with the absorption of concepts previously foreign

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

to it, and submission to external decisions with internal repercussions, of a directive nature, as in the case of the European Commission — constitutes a rupture in the then-prevailing view of sovereignty.

Thus, in a logical and interconnected sequence of phenomena, the network-based rapprochement driven by technology, together with the socioeconomic events that follow one another, shape the world within a globalized reconfiguration which, in turn, points to the integrated unification of blocs of nations as an apt strategy for confronting the corresponding challenges, while at the same time demanding a certain degree of renunciation of absolute powers as a sovereign nation — the aforementioned relativization of state sovereignty — precisely on account of the principle of cooperation and negotiated concession aimed at achieving the common objective of the whole, rather than that of a single entity (NASSER, 2021).

Nevertheless, although such premises of integration might apparently give the impression of a deconstruction of the State, the evidence in fact shows that they enhance its capacities.

Political-economic integration stimulates development through the increased circulation of goods and money, as a

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

consequence of the gains derived from specialization brought about by international negotiations and contracts, the exploitation of economies of scale, the abandonment of monopolies, and lower prices, all of which in turn bring about a social readjustment through job creation, the promotion of education, the eradication of poverty, and access to healthcare and a healthy quality of life, all stemming from the reaffirmation arising from human empowerment as a consequence of effectively guaranteed dignity (PORTO, 2017).

Moreover, it has created among the individuals belonging to that community a sense of citizenship distinct from that of their own country, reflecting a form of legitimation and appropriation that goes beyond mere political recognition (CASTELLS, 2018).

Added to this is the evidence of the meteoric development of all the Member States of the European Union since its creation, which can be corroborated by an analysis of the abundant official statistical data provided by the Eurostat website¹².

Solely for illustrative purposes in this study, three indicators will be presented by way of example:

¹²<http://ec.europa.eu/eurostat>.

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

Fig. 3: Exports of goods and services as a % of GDP



(Source:
<https://ec.europa.eu/eurostat/databrowser/bookmark/a0bf4b1d-a9f7-48e7-a38c-a25b35a0f361?lang=en>).

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

The chart above clearly shows the exponential economic growth of the European Union (represented by the blue line), including in relation to the European continent itself (shown by the brown line), through the rise in exports accompanied by GDP growth each year — with the exception of the sharp downturn caused by the Covid-19 pandemic.

Fig. 4: Unemployment rates by sex, age, and level of education (%)



European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

(Source:
<https://ec.europa.eu/eurostat/databrowser/bookmark/f9584954-5d21-49f6-bce4-2bff813be4b9?lang=en>

As a second indicator, the data above show unemployment rates within the European Union which, again with the exception of the brief period of increase and plateau caused by the Covid-19 health crisis in 2019, resumed a sharp decline in 2020.

Furthermore, whatever criteria are applied to the data, there is statistical evidence of improvement across all indicators, in every country that is part of the European Community.

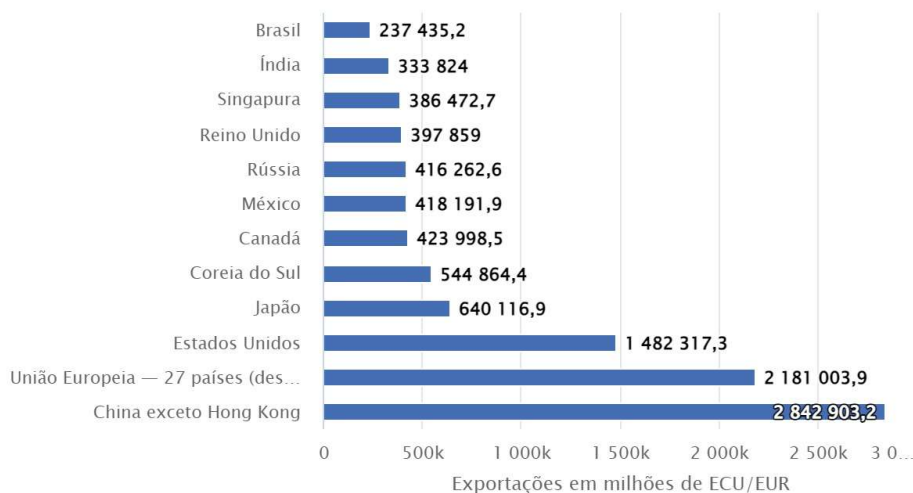
Note also the significant penetration of the European Union in world trade relative to the countries with the greatest international commercial activity (EUROPEAN UNION, 2026e):

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

Fig. 5: Figures on European Union trade

Parte da União Europeia UE27 (a partir de 2020) no comércio mundial



(Source: https://european-union.europa.eu/principles-countries-history/key-facts-and-figures/economy_pt)

The European Union today accounts for approximately 14% of world trade in goods, ranking, alongside China and the United States, among the three largest participants in international trade (EUROPEAN UNION, 2026f).

It is thus a fact that the success achieved — demonstrated here through only three indicators — shows that, combined with its intrinsic growth potential, the formation of the Community bloc has

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

proved to be a boost to the individual growth of the Member States, offering, as an integrated entity, an optimistic outlook capable of motivating the replication of this model of political-economic composition around the world.

Final Considerations

The successful recovery of the economic and political power of the European countries in less than 50 years after the devastation caused by war and destruction is certainly the fruit of an intelligent and well-articulated policy.

The conception and formation of the European Union, originating from a defensive political and economic construction born of the macro-trend toward globalization and the parallel assertion of identity as a source of meaning, thus arose from a gradual process of juxtaposing interests, negotiations, and cooperative measures aimed at a win-win outcome, pointing toward a new and prosperous model and evidencing the fact that the union of forces in pursuit of the common good is the correct path toward development.

Moreover, comparing the data presented in this study, it is certain that unification through integration presented itself to the

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

European community as a remarkable mechanism for adapting to the phenomenon of globalization which, in the wake of an installed crisis, made possible the leveraging of a new political, economic, and identity-based construction, instilling in the genesis of its nationals an autonomous European identity, parallel to the citizenship of their countries of origin.

It is evident that, being a construct intended to meet political, economic, and social expectations and purposes that are dynamic by nature, it will never attain an ideal and definitive configuration.

Yet it is precisely this capacity for perennial adaptation, made possible by the flexibility afforded by the cooperative participation of its member nations, that constitutes its greatest virtue, enabling — through its management — the harmonious conjugation and reconciliation of nations whose interests, culture, language, education, religion, and other aspects had supposedly rendered coexistence unfeasible.

In this way, the ultimate sophistication of the social and political architecture attained today by the European Union, in view of the positive results obtained, allows it to be regarded as a new paradigm of communal composition on the international stage, undoubtedly inspiring other groups of nations to consider, in light

European integration as a model of political and economic development
oriented towards globalization

DOI: <https://doi.org/10.5281/zenodo.23068475>

of their own conditions and circumstances, the formation of political and economic blocs aimed at promoting shared development.

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European integration as a model of political and economic development
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**REGULATION OF DISEASE-MODIFYING TREATMENTS
FOR ALZHEIMER’S DISEASE: A COMPARATIVE STUDY
BETWEEN THE UNITED STATES AND BRAZIL ¹**

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Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

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Abstract

Context: Alzheimer's disease is one of the greatest public health challenges of the 21st century, due to population aging and the increasing prevalence of dementia worldwide. The arrival of disease-modifying therapies, especially anti-amyloid antibodies, has reignited debates on

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Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

regulation, cost-effectiveness, and access. **Problem:** Although recent clinical results indicate progress, uncertainties remain regarding the magnitude of benefits, potential adverse risks, and, above all, the differences in regulatory models adopted by the United States and Brazil.

Objectives: This study aims to comparatively analyze the roles of the FDA and CMS, on the one hand, and Anvisa, Conitec, and ANS, on the other, highlighting approval timelines and criteria, evidentiary requirements, financial coverage policies, and access challenges. **Methods:** The research adopts a deductive approach, based on a literature review, as well as the analysis of national and international legislation, legal doctrine, and case law. It is a comparative law study in regulatory health, designed to identify convergences and divergences between the U.S. and Brazilian models.

Results: The analysis revealed that the United States applies accelerated approval pathways through the FDA, followed by clinical confirmation, with integration between regulatory processes and public coverage by CMS, although conditioned on continuous evidence generation. In Brazil, Anvisa recently approved donanemab, but the incorporation process into the SUS and by ANS is still underway, characterized by caution regarding cost-effectiveness, increasing judicialization, and structural limitations in the diagnostic network. **Conclusions:** The U.S. model ensures greater speed and integration between approval and funding, while Brazil shows regulatory progress but still faces barriers to guaranteeing broad and equitable access.

Keywords: Alzheimer's disease. Disease-modifying treatments. Health regulation. FDA. Anvisa. Comparative law. Health technology assessment.

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

Introduction

Alzheimer's disease has emerged as one of the most significant contemporary public health challenges, driven by population aging and the steadily increasing global prevalence of dementia. This scenario generates not only substantial clinical and familial burdens but also profound economic and societal consequences, threatening the sustainability of healthcare systems. Historically, available therapeutic options have been limited to symptomatic treatments aimed at partially alleviating cognitive and behavioral decline, without altering the natural course of the disease.

The advent of disease-modifying therapies—particularly monoclonal antibodies targeting amyloid-beta protein—has introduced new regulatory and ethical challenges related to the assessment of clinical efficacy, cost-effectiveness, and equitable access. As Paim (2017) argues, health regulation and policymaking should be guided by the principles of comprehensiveness, therapeutic rationality, and social justice, ensuring that the adoption of new health technologies expands rather than restricts rights. Within this framework, the present study examines how different regulatory models, particularly those adopted by the U.S. Food and Drug Administration (FDA) and the Brazilian Health

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

Regulatory Agency (Anvisa), influence the approval, adoption, and accessibility of innovative therapies for Alzheimer's disease, taking into account the strengths and limitations of each regulatory system.

A comparison of the regulatory frameworks in the United States and Brazil reveals distinct institutional approaches to health technology governance, particularly regarding the assessment of efficacy, safety, and cost-effectiveness. According to Viana (2018), health regulatory policies reflect the ways in which the state is organized and the interactions among science, the market, and the public interest, thereby explaining differences in decision-making processes and the pace of technology adoption.

In the United States, the Food and Drug Administration (FDA) has implemented accelerated approval pathways that allow earlier access to innovative therapies based on surrogate endpoints, while requiring post-marketing confirmation of clinical benefit through advanced-phase clinical trials (FDA, 2021a; FDA, 2021b). This strategy has been accompanied by timely public coverage decisions by the Centers for Medicare & Medicaid Services (CMS, 2022; CMS, 2023), illustrating a highly dynamic regulatory model characterized

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

by close integration between regulatory oversight and healthcare financing.

In Brazil, the Brazilian Health Regulatory Agency (Anvisa) is responsible for evaluating the quality, safety, and efficacy of new therapies for marketing authorization, whereas the National Commission for the Incorporation of Health Technologies into the Unified Health System (Conitec) assesses cost-effectiveness and budget impact before recommending their incorporation into the Brazilian Unified Health System (SUS) (Brazil, 2022). As noted by Ocké-Reis (2018), the Brazilian regulatory model seeks to balance innovation with the long-term sustainability of the healthcare system; however, it tends to be slower because of the institutional separation between regulatory approval, technology incorporation, and private health insurance coverage decisions by the National Regulatory Agency for Private Health Insurance and Plans (ANS, 2021). Although this institutional structure provides more rigorous technical oversight, it also extends the interval between regulatory approval and the actual availability of new treatments to patients.

As Boaventura de Sousa Santos (2002) argues, legal and institutional knowledge must be interpreted in light of its social function and the historical context in which it is produced, giving

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

international comparative analysis a critical and emancipatory dimension. Accordingly, this study adopts a qualitative, deductive approach based on a review of the literature and an analysis of national and international legislation, legal scholarship, and case law, with the objective of providing both theoretical and practical contributions to the improvement of health regulatory policies and health technology incorporation.

Against this backdrop, the present study aims to comparatively examine the regulatory frameworks and access challenges associated with disease-modifying therapies for Alzheimer's disease in the United States and Brazil, highlighting their convergences, divergences, and legal and social implications. The research is grounded in the comparative analysis of public policies and draws upon theoretical perspectives that conceptualize law as a mediating force among science, the state, and society.

Methods

This study employed an exploratory, document-based qualitative design using a comparative legal approach within the fields of Health Law and Health Regulatory Policy. As Diniz (2019) notes, scientific legal research involves the systematic analysis of

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

normative and doctrinal sources, integrating deductive reasoning with critical interpretation to understand legal phenomena within their broader social and institutional contexts. Accordingly, this investigation examines the normative, institutional, and jurisprudential foundations governing the regulation and financing of disease-modifying therapies for Alzheimer's disease through a comparative analysis of the U.S. and Brazilian regulatory frameworks.

The methodological approach combined a narrative literature review with documentary analysis, encompassing peer-reviewed scientific publications, legislation, regulatory instruments, and relevant judicial decisions. The literature search was conducted between January 2021 and September 2025 using both national and international databases, including the Virtual Health Library (VHL), SciELO, the CAPES Journal Portal, and Google Scholar, as well as institutional reports and official documents. Search terms were used in both Portuguese and English and combined with Boolean operators. These included *Alzheimer's disease, monoclonal antibodies, amyloid-beta, health regulation, coverage, cost-effectiveness, Conitec, FDA, CMS, ANS, Anvisa, and health judicialization*.

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

Eligible studies included peer-reviewed articles and technical or institutional documents addressing the regulation of health technologies, health economic evaluation, and mechanisms for coverage and access to anti-amyloid-beta monoclonal antibodies. Regulatory instruments, technical reports, and official publications relevant to the study objectives were also included, as were judicial decisions concerning access to high-cost medications. Editorials, opinion pieces lacking documentary support, non-peer-reviewed preprints, duplicate records, and materials unrelated to the study scope were excluded.

At the international level, the analysis included reports and official communications issued by the U.S. Food and Drug Administration (FDA) (2018; 2020; 2021a; 2021b; 2023; 2024) and the Centers for Medicare & Medicaid Services (CMS) (2022; 2023). In the Brazilian context, the study examined regulatory documents and publications issued by the Brazilian Health Regulatory Agency (Anvisa, 2022), the National Commission for the Incorporation of Health Technologies into the Unified Health System (Conitec, 2011; 2025), and the National Regulatory Agency for Private Health Insurance and Plans (ANS, 2021), as well as Collegiate Board Resolutions (RDCs), clinical protocols, and guidelines related to the

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

incorporation of disease-modifying therapies. The legal analysis was further supplemented by a review of recent judicial decisions concerning access to medications lacking Anvisa approval or authorized under restricted conditions, including precedents from the Federal District and Territories Court of Justice (TJDFT, 2025) and Brazil's higher courts, with the aim of examining the impact of health-related litigation on access to innovative therapies.

According to Lakatos and Marconi (2021), documentary analysis provides a means of understanding social and normative phenomena through the critical interpretation of secondary sources, making it particularly suitable for comparative legal research. Accordingly, the collected data were subjected to thematic content analysis, and a comparative analytical framework was developed to examine the United States and Brazil across four key domains: (i) regulatory pathways and approval requirements; (ii) coverage and reimbursement mechanisms, including *coverage with evidence development*; (iii) clinical evidence and cost-effectiveness assessment; and (iv) implications for patient access. The findings were synthesized through a critical comparative analysis highlighting regulatory convergences, divergences, and existing gaps. Because the study relied exclusively on publicly

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

available secondary data, it did not involve human participants and therefore did not require review or approval by a research ethics committee.

Results and Discussion

Alzheimer's disease is one of the leading causes of dementia and poses an increasing challenge to healthcare systems because of its substantial clinical, social, and economic burden. As Paim (2017) argues, addressing complex chronic conditions requires public policies grounded in the principles of comprehensiveness, equity, and therapeutic rationality to ensure that scientific progress does not become a driver of social exclusion. Within this context, the development of disease-modifying therapies, particularly monoclonal antibodies targeting amyloid-beta protein, represents a major milestone in contemporary biomedicine. Unlike conventional symptomatic treatments, these therapies are designed to target the underlying pathophysiological mechanisms of the disease, with the goal of slowing disease progression while redefining the regulatory and ethical landscape of innovation in healthcare.

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

The debate surrounding these therapies extends well beyond the biomedical domain and encompasses health regulation and public health policy, including the legal, economic, and institutional dimensions of health technology assessment and equitable access. From this perspective, the present study examines the regulatory frameworks governing anti-amyloid therapies in the United States and Brazil, focusing on the roles of the principal regulatory and reimbursement authorities—the U.S. Food and Drug Administration (FDA) and the Centers for Medicare & Medicaid Services (CMS) in the United States, and the Brazilian Health Regulatory Agency (Anvisa), the National Commission for the Incorporation of Health Technologies into the Unified Health System (Conitec), and the National Regulatory Agency for Private Health Insurance and Plans (ANS) in Brazil.

Comparative analysis emphasizes key regulatory and technical aspects, including approval timelines and criteria, clinical evidence requirements, reimbursement and coverage mechanisms, and challenges related to equitable access. The findings are derived from a comprehensive review of the scientific literature, regulatory documents, and judicial decisions and seek to elucidate how different institutional arrangements influence the effectiveness of

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

regulatory oversight and the realization of the right to health in the context of therapeutic innovation.

1. U.S. Regulatory System

In the context of Alzheimer's disease, the coordinated roles of the U.S. Food and Drug Administration (FDA) and the Centers for Medicare & Medicaid Services (CMS) have been instrumental not only in the approval of novel therapies but also in establishing access and reimbursement policies for older adults, the population most affected by the disease. As Viana (2018) argues, health regulatory systems constitute arenas in which scientific innovation, economic sustainability, and the public interest intersect, making technical decisions inherently political and socially consequential.

The FDA, an agency within the U.S. Department of Health and Human Services (HHS), plays a central role in the regulation of pharmaceuticals, medical devices, and food products in the United States. For drug approval, the agency employs multiple regulatory pathways, including traditional approval and accelerated approval. The accelerated approval pathway, established in 1992 in response to the HIV/AIDS crisis, was designed to expedite patient access to

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

promising therapies when no effective treatment alternatives are available (FDA, 2018; Friedman & Califf, 2019).

Applying this regulatory framework to Alzheimer's disease, the FDA granted accelerated approval to anti-amyloid monoclonal antibodies using the reduction of amyloid-beta plaques, measured by positron emission tomography (PET), as a surrogate endpoint (FDA, 2021b). Although this biomarker was considered reasonably likely to predict clinical benefit, the direct relationship between amyloid clearance and meaningful cognitive improvement remains the subject of ongoing scientific debate (Cummings et al., 2021).

A major regulatory milestone occurred in 2021 with the accelerated approval of aducanumab (Aduhelm), a decision that generated substantial controversy because of inconsistent clinical trial results and the negative recommendation issued by the FDA's independent advisory committee (FDA, 2021a; Knopman, Perlmutter, & Selkoe, 2021). In 2023, the FDA granted traditional approval to lecanemab (Leqembi), reinforcing the use of biomarkers as an initial regulatory criterion while emphasizing the importance of demonstrating clinically meaningful efficacy (FDA, 2023). The following year, donanemab (Kisunla) received traditional approval under a similar regulatory rationale, further establishing

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

anti-amyloid monoclonal antibodies as disease-modifying therapies for Alzheimer's disease while maintaining stringent post-marketing safety surveillance (FDA, 2024).

The FDA operates within a regulatory framework characterized by transparency and public engagement, incorporating independent advisory committee meetings, publication of scientific review documents, and opportunities for public comment (FDA, 2020). Although the agency's final decisions do not always align with the recommendations of external experts, this process enhances both the scientific credibility and institutional legitimacy of its regulatory actions and is widely regarded as an international benchmark for regulatory accountability.

Regulatory approval, however, does not automatically guarantee patient access. In the United States, reimbursement decisions are determined by the CMS, which administers Medicare, the federal health insurance program covering approximately 65 million Americans. Following the approval of aducanumab, CMS adopted a restrictive coverage policy, limiting reimbursement to patients enrolled in qualifying clinical trials because of uncertainty regarding the therapy's clinical effectiveness and its substantial cost (CMS, 2022). After the traditional approval of lecanemab, CMS

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

expanded coverage while requiring participation in national patient registries designed to monitor long-term safety and real-world effectiveness under a Coverage with Evidence Development (CED) framework (CMS, 2023).

This model reflects an effort to balance early patient access with fiscal responsibility by closely integrating regulatory approval and public reimbursement policy. Nevertheless, significant challenges remain. The high cost of disease-modifying therapies places considerable financial pressure on the Medicare program (Cubanski & Neuman, 2021), while the risk of amyloid-related imaging abnormalities (ARIA)—including cerebral edema and cerebral microhemorrhages—necessitates intensive safety monitoring and access to specialized diagnostic infrastructure (Salloway et al., 2022).

Finally, substantial structural disparities in access persist, influenced by supplemental insurance coverage, geographic location, and socioeconomic barriers. The requirement for advanced diagnostic and monitoring infrastructure, including amyloid PET imaging and serial magnetic resonance imaging (MRI), is likely to exacerbate regional disparities by concentrating access in major academic and specialized medical centers, thereby

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

reinforcing ongoing concerns regarding equity in access to biomedical innovation.

1.1. Critical Synthesis

The U.S. regulatory experience illustrates a framework characterized by procedural flexibility and the use of expedited approval pathways, particularly accelerated approval, combined with relatively efficient coordination between the U.S. Food and Drug Administration (FDA) and the Centers for Medicare & Medicaid Services (CMS) regarding reimbursement decisions. This institutional arrangement seeks to balance timely access to innovative therapies with regulatory accountability through robust post-marketing surveillance mechanisms. Nevertheless, considerable debate persists regarding whether the clinical evidence available at the time of initial approval is sufficient to justify market authorization.

This policy reflects the enduring tension among biomedical innovation, public demand for rapid access to new therapies, and the financial sustainability of healthcare systems. As Ferraz (2009) argues, judicialization and the incorporation of new health technologies without distributive criteria may create systemic

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

imbalances and exacerbate inequities in access, thereby challenging the principle of health justice. In the U.S. context, this tension is particularly evident, as the regulatory system seeks to reconcile access to innovative treatments with the long-term fiscal sustainability of Medicare, which provides coverage for the majority of eligible patients.

The case of aducanumab illustrates the vulnerabilities inherent in this regulatory model. The drug's approval based on limited clinical evidence, followed by widespread clinical skepticism and its subsequent commercial discontinuation (ICER, 2021; Alzheimer Europe, 2024), underscored the importance of transparent decision-making processes supported by robust, reproducible, and continuously reassessed evidence. In this regard, regulatory innovation must be accompanied by rigorous post-marketing surveillance to ensure that procedural efficiency does not compromise the legitimacy, credibility, or safety of regulatory decisions.

The high cost of disease-modifying therapies for Alzheimer's disease further intensifies the ethical debate surrounding distributive justice and equitable access. Their substantial financial burden places increasing pressure on public healthcare budgets

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

while creating additional socioeconomic barriers, particularly for vulnerable populations that lack access to advanced diagnostic infrastructure and specialized longitudinal care. Consequently, the U.S. regulatory framework serves as an institutional laboratory for regulatory innovation, while simultaneously exposing the structural limitations of efforts to reconcile rapid access, cost-effectiveness, and equity.

For Brazil, where the constitutional principle of universal healthcare under the Unified Health System (SUS) coexists with significant budgetary constraints, the U.S. experience offers both valuable lessons and important cautions. It demonstrates the potential benefits of more agile pathways for incorporating emerging technologies while highlighting the risks associated with accelerated regulatory decisions that may ultimately compromise the long-term sustainability and social equity of the healthcare system.

2. Regulation and Health Litigation in Brazil

In Brazil, the Brazilian Health Regulatory Agency (Anvisa) plays a central role in the regulation of new medicines, evaluating applications on the basis of quality, safety, and efficacy. The

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

enactment of Collegiate Board Resolution (RDC) No. 753/2022, which updated RDC No. 200/2017, introduced more objective and transparent prioritization mechanisms, allowing expedited review of innovative therapies and treatments intended for rare or serious diseases (Brazil, 2022). This regulatory reform, aligned with international best practices, sought to enhance regulatory predictability and strengthen health oversight while promoting the principles of rationality and administrative efficiency.

In 2025, Anvisa granted marketing authorization for donanemab (Kisunla) for the treatment of early-stage Alzheimer's disease, restricting its indication to the genetic subgroup considered at lower risk for severe adverse events (Brazil, 2025). This decision represented a regulatory milestone, marking the first approval of a disease-modifying monoclonal antibody for Alzheimer's disease in Brazil. By contrast, lecanemab (Leqembi) has not yet received marketing authorization, and the absence of regulatory approval has served as the basis for judicial decisions denying compulsory access to the therapy (TJDFT, 2025).

According to Viana (2018), health regulation is a political and institutional process that integrates scientific evidence, economic considerations, and social values. Consequently, the incorporation

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

of new health technologies should be accompanied by systemic planning and distributive criteria. Marketing authorization, although a prerequisite for commercialization, does not by itself ensure universal access. Within the Brazilian Unified Health System (SUS), the effective availability of new therapies depends on evaluation by the National Commission for the Incorporation of Health Technologies into the SUS (Conitec), established under Decree No. 7,646/2011, which assesses clinical efficacy, cost-effectiveness, and budget impact before recommending incorporation into the public healthcare system (Brazil, 2011).

The 2025 update of the Clinical Protocol and Therapeutic Guidelines (PCDT) for Alzheimer's Dementia illustrates Conitec's incremental and evidence-based approach. The expansion of donepezil eligibility to include patients with severe disease (Brazil, 2025) reflected the SUS commitment to the gradual and responsible expansion of therapeutic coverage in accordance with the best available scientific evidence, while avoiding disproportionate financial and public health risks.

This approach highlights the ethical and economic dilemma inherent in health technology incorporation within the SUS: ensuring access to innovation without compromising the long-term

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

financial sustainability of the public healthcare system. As Barroso (2021) argues, the right to health, when enforced without appropriate technical and distributive criteria, may lead to judicial decisions that disrupt public health policies and exacerbate regional inequalities. Indeed, health-related litigation has become a defining feature of the Brazilian healthcare system. The constitutional right to health, established under Article 196 of the 1988 Federal Constitution, has frequently been invoked to secure access to high-cost medications, including therapies that have not yet received Anvisa approval or have not been incorporated into the SUS or the mandatory coverage list established by the National Regulatory Agency for Private Health Insurance and Plans (ANS). This tension between legal entitlement and policy implementation reflects the ongoing challenge of balancing judicial protection of individual rights with the collective interest and the rational allocation of public resources (Barroso, 2009).

In addition, structural inequalities continue to limit access to innovative therapies. Disease-modifying monoclonal antibodies such as donanemab and lecanemab require sophisticated diagnostic and monitoring resources, including amyloid positron emission tomography (PET) imaging and serial magnetic resonance

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

imaging (MRI), which remain concentrated in major urban centers and predominantly within the private healthcare sector. According to Alencar et al. (2024), the unequal distribution of healthcare infrastructure and advanced diagnostic equipment undermines the constitutional principle of universality, widening regional disparities and restricting access in underserved areas. This raises a fundamental question of distributive justice: how can advances in biomedical innovation be translated into equitable benefits for patients across different geographic regions and socioeconomic groups? As Barroso (2021) contends, the answer lies in integrating sound technical regulation with long-term health system planning and evidence-informed public policies, ensuring that scientific innovation ultimately promotes both health equity and the effective realization of the right to health.

2.1. Critical Synthesis (Brazil)

The Brazilian regulatory landscape reflects a trajectory marked by meaningful progress alongside persistent structural challenges. Among the most significant advances are the expansion of symptomatic treatment options—including the incorporation of donepezil into the Brazilian Unified Health System (SUS) for patients

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

with severe Alzheimer's disease in 2025—and Anvisa's approval of donanemab (Kisunla) in the same year, representing the first disease-modifying therapy for Alzheimer's disease to receive marketing authorization in Brazil (Brazil, 2025). These developments demonstrate a concerted institutional effort to align clinical protocols with advances in international scientific evidence while responding to the growing societal demand for therapeutic innovation.

Despite these advances, a substantial gap remains between regulatory approval and the actual availability of therapies to patients. The health technology assessment process conducted by Conitec and reimbursement decisions involving the National Regulatory Agency for Private Health Insurance and Plans (ANS), although essential for ensuring budgetary sustainability and cost-effectiveness, often significantly delay patient access. In this respect, the pace of regulatory decision-making in Brazil contrasts with the U.S. experience, where closer coordination between regulatory approval and reimbursement has facilitated more rapid access to innovative therapies (CMS, 2023; FDA, 2024).

Another major challenge concerns the high cost of anti-amyloid monoclonal antibodies, which places considerable pressure on both

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

the SUS and the private health insurance sector. Economic impact analyses have shown that therapies of this nature may threaten the long-term financial sustainability of universal healthcare systems, particularly in middle-income countries such as Brazil (Friedman & Califf, 2019; ICER, 2021). Consequently, decisions regarding the incorporation of these technologies require a careful balance between fostering biomedical innovation and maintaining fiscal responsibility.

An additional concern relates to the need for highly specialized diagnostic and monitoring infrastructure, including amyloid positron emission tomography (PET) imaging and serial magnetic resonance imaging (MRI). As reported by Alencar et al. (2024), these resources remain concentrated primarily in Brazil's South and Southeast regions, reinforcing longstanding regional disparities in healthcare infrastructure. As a result, even when incorporated into clinical practice, these novel therapies are likely to benefit predominantly patients receiving care in large urban centers, thereby limiting both geographic and socioeconomic equity in access.

From a legal perspective, health-related litigation continues to play a central role in shaping access to high-cost therapies.

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

Although litigation serves as an important mechanism for enforcing the constitutional right to health established under Article 196 of the Federal Constitution, it may also generate systemic distortions by prioritizing individual claims over technically grounded and collectively oriented public health policies (Barroso, 2009). Judicial decisions have varied between ordering immediate access to innovative therapies and reaffirming the prohibition against publicly funding medications that have not received Anvisa approval, illustrating the ongoing tension between regulatory legality and urgent societal demands.

This dilemma underscores the need for stronger institutional coordination among the judiciary, regulatory agencies—including Anvisa, Conitec, and ANS—and administrators of the SUS. Only through such integrated governance can the protection of individual rights be reconciled with the requirements of fiscal sustainability and evidence-based public policymaking, thereby fostering judicial decisions that are both scientifically informed and socially balanced.

From an analytical perspective, the Brazilian experience represents a paradigmatic example of the tension among scientific innovation, fiscal responsibility, and distributive justice. On the one

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

hand, substantial regulatory advances have been achieved in establishing pathways for the incorporation of disease-modifying therapies for Alzheimer's disease. On the other hand, persistent structural barriers continue to impede the translation of these regulatory milestones into equitable and effective patient access. Addressing this challenge will require the development of integrated public policies grounded in rigorous cost-effectiveness analyses, robust clinical evidence, and sustainable financing strategies. Only through such a coordinated approach will it be possible to establish a responsible framework for health technology incorporation that promotes equitable access, efficient stewardship of public resources, and the ethical, rational, and socially just realization of the constitutional right to health.

3. Regulation and Access: Contrasting the United States and Brazil

In the United States, regulatory decisions are generally reached more rapidly, largely because of the accelerated approval pathway, a mechanism established in 1992 in response to the HIV/AIDS crisis and subsequently applied to Alzheimer's disease. This pathway allows earlier authorization of promising therapies in areas of

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

significant unmet medical need by accepting surrogate endpoints, such as reductions in amyloid-beta plaque burden, as evidence reasonably likely to predict clinical benefit. It was through this mechanism that the FDA approved aducanumab in 2021, a decision that generated substantial controversy because of the lack of scientific consensus regarding the relationship between biomarker reduction and meaningful cognitive improvement (FDA, 2018; Cummings et al., 2021).

In contrast, Brazil follows a more sequential and cautious regulatory process, as illustrated by Anvisa's approval of donanemab (Kisunla) in 2025. The agency restricted the indication to specific genetic subgroups—patients who are either non-carriers or heterozygous carriers of the APOE ϵ 4 allele—owing to differences in the risk of serious treatment-related adverse events. This decision reflects a more conservative regulatory approach that conditions patient access on robust clinical evidence while prioritizing patient safety (Brazil, 2025). Thus, whereas the U.S. model emphasizes regulatory flexibility and timely access to innovation, the Brazilian framework places greater weight on precaution and the protection of public health.

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

A further distinction concerns the evidentiary standards required for regulatory approval. Initially, the FDA accepted biological surrogate markers as sufficient evidence of therapeutic efficacy despite the absence of definitive proof of clinically meaningful cognitive benefit. By contrast, Anvisa adopted a more stringent position, requiring stronger clinical evidence before granting marketing authorization. This divergence reflects not only different regulatory philosophies but also the realities of Brazil's universal publicly funded healthcare system, in which each regulatory decision has direct implications for the long-term financial sustainability of the Brazilian Unified Health System (SUS).

According to Ferreira and Magalhães (2020), health-related litigation in Brazil highlights persistent gaps between health regulation and public policymaking, revealing insufficient integration between scientific and legal decision-making. The authors argue that the fragmented operation of these sectors encourages reactive and isolated decisions, ultimately undermining both the effectiveness of access policies and the rational incorporation of new health technologies. From this perspective, Anvisa's cautious regulatory stance represents not merely a technical choice but also an institutional response aimed at

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

ensuring therapeutic safety and distributive justice within a universal public healthcare system.

Differences between the two countries become even more apparent with respect to reimbursement and healthcare financing. In the United States, the Centers for Medicare & Medicaid Services (CMS) implemented the Coverage with Evidence Development (CED) policy, which provides conditional reimbursement for selected therapies while requiring the systematic collection of real-world evidence through national patient registries. This approach links early patient access to continuous evaluation of long-term effectiveness and safety (CMS, 2023; *Health Affairs*, 2023). In Brazil, public reimbursement depends on cost-effectiveness and budget impact assessments conducted by Conitec, while coverage decisions within the private healthcare sector are made by the National Regulatory Agency for Private Health Insurance and Plans (ANS). Although these processes are essential for ensuring the efficient allocation of public resources, they are typically more complex and time-consuming, often prompting patients to seek judicial intervention as an alternative means of obtaining access to therapies that have not yet been incorporated into coverage policies.

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

Despite their structural and regulatory differences, both countries face similar challenges regarding financial sustainability and healthcare infrastructure. In the United States, the high annual cost of anti-amyloid monoclonal antibodies places substantial pressure on the Medicare budget, limiting the widespread adoption of these therapies (Cubanski & Neuman, 2021). In Brazil, the barriers are even more pronounced. Beyond the economic burden, the effectiveness of these treatments is constrained by the limited availability of specialized diagnostic infrastructure, particularly amyloid positron emission tomography (PET) imaging and serial magnetic resonance imaging (MRI). These resources remain concentrated primarily in the South and Southeast regions, contributing to significant geographic and socioeconomic disparities in access to specialized care (Alencar et al., 2024).

Overall, the comparative analysis of the U.S. and Brazilian regulatory and reimbursement frameworks demonstrates that the U.S. system prioritizes the rapid adoption of innovative technologies, albeit with a greater degree of regulatory uncertainty, whereas the Brazilian model emphasizes cautious decision-making and patient safety, constrained by structural and fiscal limitations. Despite these differences, both countries confront the same

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

fundamental challenge: reconciling the incorporation of innovative biomedical therapies with the long-term financial sustainability of their healthcare systems while upholding the principle of distributive justice, a cornerstone of contemporary health law and health policy.

4. Comparative Analysis of the U.S. and Brazilian Regulatory Frameworks

The analysis presented in the preceding sections demonstrates that both the United States and Brazil have established regulatory mechanisms for the approval and incorporation of novel therapies for Alzheimer's disease. Nevertheless, each system reflects the distinctive institutional, economic, and legal characteristics of its respective healthcare environment, resulting in different pathways for regulatory approval, reimbursement, and patient access.

According to Caetano et al. (2021), "health regulation and health technology incorporation are complex and dynamic processes that integrate scientific, economic, and social dimensions" (p. 5428). This perspective underscores that comparisons between regulatory systems should extend beyond their formal legal frameworks to encompass the institutional

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

culture and structural determinants that shape regulatory decision-making in each country.

To facilitate a clearer and more systematic comparison, the following section summarizes the principal similarities and differences between the United States and Brazil with respect to their regulatory frameworks, health technology incorporation processes, and the practical conditions governing patient access to disease-modifying therapies for Alzheimer's disease.

Table 1. Comparison of Regulatory Pathways for Alzheimer's Disease Therapies in the United States and Brazil

Aspect	United States	Brazil	
Regulatory authority	The FDA (Center for Drug Evaluation and Research [CDER]) employs both accelerated and traditional approval pathways. Recent approvals include Leqembi (traditional approval, 2023) and Kisunla (2024).	Anvisa regulates drug approval under RDC No. 753/2022 (which revised RDC No. 200/2017). Kisunla received marketing authorization on April 22, 2025, whereas Leqembi has not yet received regulatory approval.	
Public coverage	Medicare/CMS expanded coverage for Leqembi following its	Conitec avalia custo-efetividade e impacto Conitec evaluates cost-effectiveness and budget impact	

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

	traditional FDA approval, contingent upon patient enrollment in a national data registry.	before therapies can be incorporated into the Brazilian Unified Health System (SUS) under Decree No. 7,646/2011. Donepezil for severe Alzheimer's disease was incorporated in 2025, whereas anti-amyloid therapies have not yet been incorporated.	
Risk management and monitoring	Clinical protocols require serial MRI monitoring for amyloid-related imaging abnormalities (ARIA), with risk stratification based on APOE ε4 status. These requirements are reflected in prescribing information and clinical practice guidelines.	The Brazilian prescribing information for Kisunla includes restrictions based on APOE ε4 genotype and specifies monitoring requirements, creating additional demands for advanced diagnostic infrastructure within the healthcare system.	
Speed of access	The accelerated approval pathway enables earlier patient access while confirmatory evidence is generated. Coordination between the FDA and CMS facilitates more rapid implementation of coverage decisions.	Following marketing authorization, patient access depends on multiple decision-making bodies (Anvisa, Conitec/SUS, and ANS), which may prolong access timelines and contribute to increased health-related litigation.	

Source: Prepared by the authors

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

The comparative analysis of the regulatory frameworks in the United States and Brazil reveals legal and public policy implications of considerable importance for public health and health law. The case of aducanumab (Aduhelm), approved by the FDA in 2021, represents a paradigmatic example of the risks associated with relying on surrogate endpoints as the basis for regulatory approval without robust confirmation of clinically meaningful benefit. Although the initial authorization generated considerable expectations among patients and their families, the limited strength of the supporting clinical evidence ultimately led to restricted Medicare coverage and the drug's subsequent commercial discontinuation. This trajectory underscores the importance of regulatory prudence and rigorous scientific standards when granting early access to therapies that lack well-established empirical evidence (Alzheimer's Association, 2024).

Another important consideration concerns the integration of regulatory approval and reimbursement policy. In the United States, close institutional coordination between the U.S. Food and Drug Administration (FDA) and the Centers for Medicare & Medicaid Services (CMS) allows regulatory approval to be followed rapidly by conditional public reimbursement through Coverage with

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

Evidence Development (CED), under which continued access is linked to the systematic collection of additional clinical evidence. By contrast, the Brazilian system separates regulatory approval from health technology incorporation: marketing authorization is the responsibility of Anvisa, whereas decisions regarding reimbursement and incorporation into the public and private healthcare systems are made by Conitec and the National Regulatory Agency for Private Health Insurance and Plans (ANS), respectively. This institutional separation lengthens the overall decision-making process and contributes to increased health-related litigation, as patients frequently seek judicial remedies to obtain access to therapies that have not yet been incorporated into coverage policies (Brazil, 2011; CMS, 2023). Within this context, the central legal challenge lies in balancing the collective interests of public health protection and fiscal sustainability with the immediate realization of the individual right to health.

Beyond regulatory considerations, significant structural and logistical challenges remain regarding the healthcare infrastructure required to implement disease-modifying therapies for Alzheimer's disease. Dependence on advanced diagnostic technologies—including amyloid positron emission tomography (PET) imaging and

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

serial magnetic resonance imaging (MRI) for the detection and monitoring of amyloid-related imaging abnormalities (ARIA)—creates substantial barriers to access in both countries. In the United States, these obstacles are primarily associated with socioeconomic and geographic disparities, whereas in Brazil they reflect the concentration of advanced diagnostic resources in the South and Southeast regions, together with shortages of specialized healthcare professionals in underserved areas (Alencar et al., 2024).

From this perspective, even following regulatory approval and potential incorporation of therapies such as donanemab, there remains a substantial risk that effective access will continue to be concentrated in major urban centers, thereby reproducing longstanding patterns of geographic inequality and socioeconomic exclusion (PMC, 2023). Consequently, therapeutic innovation may paradoxically reinforce the very health inequities that universal healthcare systems seek to reduce.

Overall, the legal and public policy implications of regulating disease-modifying therapies for Alzheimer's disease extend well beyond the question of marketing authorization. The contemporary challenge is to reconcile the responsible incorporation of biomedical innovation with fiscal sustainability and distributive

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

equity, ensuring that the constitutional right to health is realized in a manner that is universal, safe, evidence-based, and socially just.

Conclusion

The comparative analysis of the regulatory frameworks governing disease-modifying therapies for Alzheimer's disease in the United States and Brazil highlights both significant progress and persistent structural challenges. The U.S. model, characterized by the FDA's expedited approval pathways and close institutional coordination with the Centers for Medicare & Medicaid Services (CMS), has demonstrated a strong capacity to facilitate the early introduction of innovative therapies. At the same time, this regulatory agility exposes important scientific and economic risks, particularly when approval decisions rely on clinical evidence that remains preliminary. The case of **aducanumab** exemplifies these concerns, as its early approval generated substantial controversy regarding both its clinical effectiveness and the long-term sustainability of public reimbursement.

In Brazil, meaningful regulatory advances have been achieved through Anvisa's approval of **donanemab** and the revision of clinical protocols governing symptomatic therapies for Alzheimer's

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

disease. Nevertheless, the slow pace of health technology incorporation, the high cost of innovative treatments, and persistent structural and regional disparities continue to constrain both the effectiveness of implementation and equitable patient access. These findings suggest that the principal challenge extends beyond the formal approval of new therapies to the development of public policies capable of ensuring social effectiveness, financial sustainability, and distributive justice.

From a legal perspective, both regulatory systems confront similar challenges in balancing the right to health with the competing demands of biomedical innovation, fiscal responsibility, and social justice. In the United States, debate has centered on the speed of regulatory approvals and their budgetary implications for Medicare. In Brazil, concerns have focused on the lengthy technology incorporation process and the growing reliance on health-related litigation as a means of obtaining access to therapies that have not yet been incorporated into public or private coverage. In both settings, regulatory approval alone is insufficient when not accompanied by coordinated policies addressing reimbursement, healthcare planning, and service delivery infrastructure. These

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

findings underscore the importance of integrated governance and institutional coordination in health policy.

The evidence presented in this study indicates that the contemporary challenge of health regulation extends well beyond the binary decision of whether to approve or reject new medicines. Rather, it requires institutional, economic, and social conditions capable of translating regulatory advances into timely, safe, and equitable access to care. In the Brazilian context, achieving this objective will require the combination of scientifically rigorous regulation, expanded diagnostic capacity, fair and sustainable pricing strategies, and continued strengthening of the Brazilian Unified Health System (SUS) as a universal and redistributive public healthcare system.

From the perspective of comparative law, the experiences of the United States and Brazil demonstrate that neither regulatory model is without limitations; however, each offers valuable and complementary lessons for improving health policy in the era of biomedical innovation. The U.S. framework illustrates the benefits of regulatory agility and early access, albeit accompanied by greater clinical uncertainty and substantial financial pressures. By contrast, the Brazilian model emphasizes gradual implementation,

Regulation of disease-modifying treatments for Alzheimer's disease: a comparative study between the United States and Brazil

DOI: <https://doi.org/10.5281/zenodo.23068614>

regulatory caution, and equity, although its effectiveness continues to be constrained by structural barriers and persistent regional disparities.

Ultimately, the comparison between these two regulatory systems reaffirms that the central challenge lies not in the regulatory act itself but in the effective realization of the right to health. The future of public policies for Alzheimer's disease will depend on the ability to reconcile scientific innovation, fiscal responsibility, and social justice, ensuring that advances in biomedicine are translated into meaningful and equitable health benefits for the population as a whole rather than remaining accessible only to selected groups.

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