Department of Health and Human Services

DEPARTMENTAL APPEALS BOARD

Appellate Division

In the Case of:	DATE: May 3, 2010
In re CMS LCD Complaint:	
	Civil Remedies CR1989
Homeopathic Medicine and Transfer Factor (LCD Database ID No. L26134 (Retired))	App. Div. Docket No. A-09-123
	Decision No. 2315
Contractor: NHIC (Carrier)	
Homeopathic Medicine and Transfer Factor (LCD Database ID No. L28267 (Active))	
Contractor: Palmetto GBA (MAC)	
Oversight Region I	

FINAL DECISION ON REVIEW OF ADMINISTRATIVE LAW JUDGE DECISION

The Aggrieved Parties (APs), through their representative, Dorothy Calabrese, M.D., appeal the August 11, 2009 decision of Administrative Law Judge (ALJ) Keith W. Sickendick. Homeopathic Medicine and Transfer Factor (LCD Database ID No. L28267), DAB CR1989 (2009) (ALJ Decision). In that decision, the ALJ rejected the APs' challenge to a local coverage determination (LCD) issued by a Medicare contractor that restricted coverage of transfer factor immunomodularity therapy (TF therapy).

The ALJ determined that the record before him was complete and adequate to support the validity of the LCD provision at issue

under the reasonableness standard set forth at section 1869(f)(2)(A) of the Social Security Act (the Act) (42 U.S.C. § 395ff(f)(2)(A)). The ALJ also determined that additional arguments made by the APs were without merit or beyond his authority to review because they were unrelated to the issue of whether the LCD record was complete and adequate to support the validity of the LCD.

The ALJ did a thorough and persuasive job of reviewing and ruling on the evidentiary and procedural complexities presented by the case. For the reasons discussed below, we conclude that the APs have failed to demonstrate any basis for reversing the ALJ Decision, and we uphold it in full.

Background

1. LCDs

Section 1869(f)(2)(B) of the Act defines an LCD as "a decision by a [contractor] under Medicare . . . Part B . . . respecting whether or not a particular item or service is covered on a [contractor-]wide basis . . . in accordance with section 1862(a)(1)(A)."[1] See also 42 C.F.R. § 400.202. With certain exceptions not relevant here, section 1862(a)(1)(A) specifies that no Medicare payment may be made for items and services which "are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member." The coverage exclusion in section 1862(a)(1)(A) is sometimes referred to as the "medical necessity" standard.

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[1] As the ALJ stated, subsection 1869(f) was "added to section 1869 of the Act by the Benefit Improvement and Protections Act of 2000 (BIPA), Pub. L. 106-554 § 522." ALJ Decision at 13 n.9. The APs rely on section 1869(f) in many arguments but cite it as "BIPA 2000 Sec 522." The appeal request states that the ALJ "never mentions BIPA 2000 Sec 522 anywhere in his decision." Appeal Request (AR) at 35. In fact, the ALJ relies on "BIPA 2000 Sec. 522" throughout his decision but cites it as section 1869(f), as do we. An LCD is distinct from a national coverage determination (NCD), which section 1869(f)(1)(B) defines as "a determination by the Secretary with respect to whether or not a particular item or service is covered nationally under this title . . . ."

As the ALJ explained, the appeal process for denials of individual claims (which may result from application of an LCD or from many other considerations) is separate from the administrative process for challenges to the LCD policies themselves. ALJ Decision at 12-13, and citations therein. A beneficiary (or in some cases provider or supplier) whose claim is denied, whether because the contractor finds that the service was not medically necessary or for other reasons, may seek review of that denial in accordance with procedures set out in 42 C.F.R. Part 405, subpart I (for original Medicare claims under Parts A and B). Claims appeals focus generally on whether the individual beneficiary actually needed the item or service, all requirements for payment were met (such as documentation), and other aspects of the individual claims at issue were established. Claims denial decisions may be appealed, in appropriate circumstances, to the ALJs of the Office of Medicare Hearings and Appeals (OMHA) and then to the Medicare Appeals Council (MAC). See generally 42 C.F.R. § 405.1000-1140. The resolution of a claims denial appeal impacts only those who are parties to the claims appeal.

The basis for a contractor's claims denial may be that an LCD bars coverage of the item or service for the purpose claimed. However, LCDs are not binding beyond the issuing contractor, although they are entitled to substantial deference. 42 C.F.R. § 405.1062. Hence, the administrative entities that review the contractor's determination to deny a Medicare claim based on an LCD, i.e., OMHA's ALJs or the MAC, may conclude in appropriate circumstances that the service at issue was medically reasonable and necessary for that individual claimant and reverse the contractor's denial of the claim despite the LCD. (LCDs differ in this regard from NCDs which are binding at all levels of administrative review. 42 C.F.R. § 405.1060(a)(4); 68 Fed. Reg. 63,692, at 63,693 (2003).) Such a decision would not, however, result in the LCD being held invalid and would not mean that other beneficiaries (or even the same beneficiary in a future case) would have their claims covered even if they were similarly situated.

The LCD challenge process is governed by 42 C.F.R. Part 426. These cases are initiated by a complaint to an ALJ in the Civil Remedies Division of the Departmental Appeals Board (DAB). 42 C.F.R. § 426.300. ALJ decisions on the validity of LCDs are appealable to the Board. 42 C.F.R. § 426.465. In LCD challenges, the treating physician's statement is accepted as sufficient to establish the beneficiary's need for coverage as required for standing as an aggrieved party, without any factual

inquiry into the medical records of the individual beneficiaries bringing the case. 42 C.F.R. §§ 426.110, 426.400(b)(3), 426.410(b)(1). A beneficiary is required only to identify the service that is needed and explain why it is unreasonable to have a policy denying coverage in order to challenge an LCD provision. 42 C.F.R. § 426.400(b)(5). The focus is not on the individual's circumstances or treatment but on whether the challenged policy provision precluding coverage is valid. The aggrieved party thus is allowed to submit clinical and/or scientific evidence and to explain why that evidence shows that the noncoverage provision in the LCD is unreasonable. 42 C.F.R. § 426.400(b)(6). Also, aggrieved parties may file joint complaints (as they have done here) when they have similar medical conditions and challenge the same LCD provisions. 42 C.F.R. § 426.400(d). The result of the LCD challenge process may impact other similarly-situated beneficiaries if an LCD is found invalid. 68 Fed. Reg. at 63,694.

2. Case History

Below, we set forth a brief history of proceedings before the Civil Remedies Division ALJs and before this Board involving challenges to LCDs restricting reimbursement for TF therapy. (The ALJ Decision contains a more comprehensive history of related litigation.) The entities defending the validity of the LCD provisions in these proceedings have been the National Heritage Insurance Company (NHIC) and Palmetto GBA (Palmetto), Medicare contractors, and the Centers for Medicare & Medicaid Services (CMS).[2] The private parties have been various APs represented (and treated) by Dr. Calabrese. Only Medicare beneficiaries in need of the items or services that are the subject of an LCD noncoverage provision have standing to challenge it and are defined by the implementing regulation as "aggrieved part[ies]." Section 1869(f)(5) of the Act; 42 C.F.R. § 426.110. Dr. Calabrese is a physician in California who advocates and uses TF therapy for the treatment of patients with

[2] NHIC was initially the representative of the federal interest in this proceeding. CMS entered an appearance on August 26, 2008 and represented the federal interest thereafter. CMS letter dated August 26, 2008 (item 52 in CRD record index). Palmetto never entered an appearance in the case but adopted the version of the LCD which was in force as of the time the ALJ reached his decision.

"allergies, including allergic hypersensitivity to chemicals, and abnormal cell-mediated immunity/delayed type hypersensitivity," including all of the APs. ALJ Decision at 3 (emphasis added).[3]

In 2005, multiple APs, through their representative who was also Dr. Calabrese, filed an LCD complaint with the DAB Civil Remedies Division ALJs, which was docketed as C-05-183. Those APs asserted that an article, which was posted on the NHIC website and stated that TF therapy was not covered by Medicare, constituted an LCD. They challenged the validity of the alleged LCD. The ALJ in that matter, Richard J. Smith, dismissed the case citing two alternative grounds. First, he held that the posted article did not contain an LCD as defined by the applicable law and regulations. In the alternative, he held that, even if the article had contained an LCD when the APs filed the challenge, NHIC had subsequently withdrawn the LCD by issuing a revised version of the article that did not contain the challenged provision. In re CMS LCD Complaint: Non-Coverage of Transfer Factor, DAB CR1396, at 3 (2006), citing 42 C.F.R. § 426.420(e)(1).

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[3] Dr. Calabrese does not have standing as a party in this case. The ALJ recognized that she has a real interest in the proceeding as the treating physician and as a prominent supporter of TF therapy. ALJ Decision at 21. The ALJ referred to Dr. Calabrese (rather than the APs) as the proponent of various motions and objections, accepted her factual representations and considered her opinions as proffered. Id. at 2-11, 42. He stated that he allowed her "leeway" in her presentation because she is not an attorney, noting that he did not hold her "to the standards and norms of conduct that are expected from a practitioner." Id. at 36. Many of the submissions consist of documents in the form of sworn statements and declarations by Dr. Calabrese, including the entire 437-page appeal request to the Board in the present case. We follow the ALJ's example in accepting her submissions, even though they include her statements of personal knowledge and her opinions as well as the arguments she made as the representative of the APs. While we have accepted this rather muddled presentation in this unique instance, we do not imply that aggrieved parties are entitled of right to co-mingle in their submissions opinions of an expert witness, assertions by a fact witness based on personal knowledge, and arguments of a representative.

The APs appealed ALJ Smith's decision to the Board in a case docketed as A-06-43. On October 12, 2006, the Board ruled that the noncoverage policy set forth in the challenged article did constitute an appealable LCD. LCD Appeal of Non-Coverage of Transfer Factor, DAB No. 2050 (2006). (The policy set forth in that article is referred to herein as the "First LCD.") The Board upheld, however, the ALJ's dismissal of the APs' challenge on the second ground because the Board agreed that NHIC had revised the article to remove the noncoverage policy and thus had withdrawn the LCD. Specifically, the Board concluded that the revised article (Article for Transfer Factor - Correct Coding and Recent Medical Reviews - Revised (A38251/A38252)) did not contain an LCD and reflected instead the withdrawal of the First LCD. Id. at 12.[4]

In Docket No. A-06-43, the APs also argued that, despite the revised language in A38251/A38252, NHIC intended to "to retain the contractor-wide noncoverage policy in a form inaccessible to challenge" by "continu[ing] the LCD in effect secretly." Id. at 17. The Board rejected the APs' position, stating it would not presume that NHIC would act in bad faith by denying claims for TF therapy on a contractor-wide basis under A38251/A38252. Id. The Board stated that, because NHIC had withdrawn the First LCD, "the aggrieved parties are entitled to have their prior claims reopened and readjudicated with no regard given to the withdrawn policy and . . . future claims by them or by other beneficiaries (after the effective date of the withdrawal) must be decided by NHIC without any reliance on the withdrawn policy." DAB No. 2050, at 18, citing 42 C.F.R. §§ 426.420(a), 426.460(b).

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[4] We note here that ALJ Sickendick incorrectly characterized as dictum the Board's conclusion in DAB No. 2050 that NHIC had issued an LCD by posting the noncoverage policy for TF therapy as an article on its website (i.e., First LCD). ALJ Decision at 20. The Board reached the question of whether the withdrawn policy constituted an LCD because the withdrawal of an LCD has the same legal consequences for an aggrieved party as the invalidation of an LCD. 42 C.F.R. § 426.460(a). If the Board had agreed with the ALJ that no LCD ever existed, the APs would not have been entitled to the relief provided by regulation when an LCD is withdrawn during the pendency of an appeal. The Board's conclusion was thus legally significant and not dictum.

On October 31, 2007, Dr. Calabrese was the authorized representative of one Medicare beneficiary who filed a second LCD complaint before the Civil Remedies Division, which was docketed as C-08-72.[5] The complaint alleged that NHIC was following a "'*sub rosa*' policy to automatically deny all TF claims." ALJ Decision at 23 (italics in original; footnote omitted). The case was assigned to ALJ Sickendick. The ALJ advised Dr. Calabrese of the reasons the complaint was unacceptable under the applicable regulations and informed her that NHIC had issued an LCD numbered L26134, effective October 28, 2007 and titled "Homeopathic Medicine and Transfer Factor." (LCD L26134 is referred to herein as the "Second LCD.") He further informed her that she could file an amended complaint before him. In January 2008, the APs filed an amended complaint alleging that, since October 30, 2003, NHIC had applied a contractor-wide policy to deny payment for TF therapy and that this constructive LCD continued until the contractor issued LCD L26134, the Second LCD. Id. at 2-3. The ALJ found the amended complaint to be acceptable and ordered NHIC or CMS to file the record for the Second LCD and any "predecessor constructive contractor-wide policy." Id. at 3.

On February 29 and March 1, 2008, NHIC filed its record for the Second LCD and a memorandum denying the existence of an LCD prior to the adoption of the Second LCD. Memorandum Regarding Non-Existence of LCD . . . Prior to LCD L26134 [Second LCD] (item 29 in CRD record index).

In September 2008, Palmetto replaced NHIC as the Medicare contractor responsible for California. NHIC retired LCD L26134 (the Second LCD) effective September 1, 2008 and, effective the next day, Palmetto issued LCD L28267, "Homeopathic Medicine and Transfer Factor." (LCD L28267 is referred to herein as the "Third LCD.") The ALJ determined that, because the Third LCD effectively constituted a revision of the Second LCD (rather than an entirely new LCD), the action before him should continue as a review of the Third LCD. ALJ Decision at 4, citing 42 C.F.R. § 426.420(e)(2).

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[5] Subsequently, Dr. Calabrese filed documents as the authorized representative of ten additional Medicare beneficiaries whom the ALJ accepted as APs. ALJ Decision at 2 n.1. Dr. Calabrese is also the treating physician for all 11 APs in the present appeal. Id.

CMS filed Exhibits 1 through 22. The ALJ excluded CMS Exhibits 1-3 and the first two pages of Exhibit 10, based on the APs' objections, and admitted the remainder. Id. at 10. The APs filed Exhibits 1 through 235, and the ALJ admitted them without objection. Id. at 6-7. The ALJ admitted one exhibit as Court Exhibit 1. The parties submitted multiple motions and briefs.

On August 11, 2009, the ALJ ruled against the APs, concluding that the record before him was complete and adequate to support the validity of the Third LCD under the applicable reasonableness standard set forth at section 1869(f)(2)(A) of the Act. The ALJ rejected multiple additional arguments raised by Dr. Calabrese on behalf of the APs as without merit or irrelevant. The APs filed this appeal.

3. Scientific background information on TF therapy

In order to provide some orientation to our discussion of the scientific evidence, we briefly explain here some of the terminology and concepts involved. We draw for this purpose on the arguments and supporting evidence submitted by the APs and not contested by CMS.

The adaptive immune system divides into "humoral immunity" and "cellular immunity" which function through different channels and cell lines, primarily divided into B cells and T cells. AR at 145. Humoral immunity is governed by white blood cells (lymphocytes) that mature in the bone marrow and are called B cells. Document titled "Cytokines" identified in AP Index as L. Borish, Cytokines - update, in W. B. Saunders, Allergy: Principles and Practice 10 (2008) (A.P. Ex. 148)(Borish on Cytokines). B cells produce antibodies. Id.

T cells are a different lineage of lymphocytes that mature in the thymus. Id. at 11. Cellular immunity involves any immune response where T cells react in a manner targeted to a specific antigen. J.W. Steinke and L. Borish, Cytokines and chemokines, 117 Journal of Allergy and Clinical Immunology 441-45 (2006)(A.P. Ex. 149). Antigens are substances which the body can recognize and react to as foreign to itself. Many different kinds of T cells exist. The T cells that are most relevant here are called "helper T cells" or Th cells, which in turn fall into various subsets, including Th1 and Th2 cells. AR at 118. Dr. Calabrese asserts that TF therapy modulates how Th1 cells respond to antigens. AR at 121. Dr. Calabrese's treatment protocols aim to rebalance the Th1 and Th2 responses in her patients. AR at 122-24.

Immune responses can be regulated by "cytokines," which are proteins secreted by cells in the immune system. Borish on Cytokines at 2. Cytokines carry signals between cells to influence their behavior. AR at 120. In early research, the nature of the individual proteins causing changes in immune response could not be identified and they were referred to simply as "factors" according to their observed activities. Id. at 2-3. Later research used improved protein purification and gene sequencing to elucidate the multiple activities of specific proteins. Id.

"Transfer factor," as relevant here, refers to one or more substances derived from donor blood that are alleged to convey to a recipient certain aspects of the donor's immunological capacity, a process known as "passive transfer." AR at 171. The immune response transferred to the recipient, according to the literature provided by the APs, is not driven by antibodies (produced by B cells) but rather a delayed hypersensitivity response mediated by certain T cells. Delayed hypersensitivity develops as an inflammatory response at the site of antigen contact over hours or days after exposure, with a common example being poison ivy dermatitis. C. Kirkpatrick, Delayed Hypersensitivity in Immunological Diseases, 4th ed., Vol. 1, at 261 (1988)(A.P. Ex. 1).

Dr. Calabrese states that she uses pooled blood from 33 healthy human volunteer donors to obtain the TF she uses for therapy. AR at 134. Licensed blood banks "select specific donors and specially prepare the required buffy coats . . . ." AR at 15. "Buffy coat" refers to a component of the blood separated to pull out white blood cells (leukocytes) and leave behind most red blood cells and fluid. Dr. Calabrese then processes this material by destroying the membranes of the white blood cells to release their contents into solution."[6] See, e.g., AR at 174. The solution is subjected to extensive filtration which eliminates large molecules, including antibodies, and "intense preparation including freeze drying/freeze thaw cycles" ending

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[6] While the record contains numerous reference to Dr. Calabrese's methods and those of various researchers, no complete description of the process used to create the products provided to the APs appears. Dr. Calabrese states that "there are different protocols for different classes of patients." AR at 174.

in frozen storage until use. Id. at 175. The resulting solution contains TF, which is then injected into Dr. Calabrese's patients. Dr. Calabrese uses twice-weekly injections for a three-year course of therapy, which she asserts is most likely in her experience to achieve long-lasting results, although about 10% of her patients stay on TF therapy long-term. AR at 206-07.

The LCD at issue concludes that TF therapy is not a covered service for any specific illnesses. The APs here, however, challenge the LCD for unreasonably precluding coverage of TF therapy as a treatment for their clinical conditions. Dr. Calabrese represents that all of the APs suffer clinically from "severe combined abnormal Th1 - Th2 [cell] immunoregulatory defect," often including extensive allergies to mold, foods, and chemicals. AR at 2, 104, 126, 173-74. Because they thus suffer from similar medical conditions and challenge the same LCD provision, the APs were properly permitted to pursue this challenge in a single proceeding under 42 C.F.R. § 426.400(d).

Analysis

1. The scope of the ALJ's review of an LCD, the standard for that review, the process for that review, and the Board's review of the ALJ Decision are governed by statute and regulation, by which the ALJ and the Board are bound.

The scope of the ALJ's review of the validity of an LCD and the standard and process by which that review is conducted are governed by statute and regulation. Section 1869(f)(2) of the Act establishes a two-phase LCD review process before the ALJ and provides for further appeal to the Board. The ALJ first reviews the LCD to determine whether "the record is incomplete or lacks adequate information to support the validity of the determination." If the ALJ determines that the record is incomplete or inadequate to support the validity of the determination, then further process before the ALJ including discovery and the taking of evidence is required (although that process is not specified in detail by the statute). Section 1869(f)(2)(A)(i) of the Act; 42 C.F.R. § 426.425(c)(3). The regulations do not contemplate discovery or a formal evidentiary hearing during the first phase review. 68 Fed. Reg. at 63,700, 63,710. If the ALJ determines the record is complete and adequate, however, the ALJ review process is concluded.

To resolve whether the record is complete and adequate to support the LCD, section 1869(f)(2)(A)(i)(I) directs the ALJ to

review the "reasonableness of the determination" of the contractor on which the validity of the LCD is based. Section 1869(f)(2)(A)(i)(III) of the Act also requires the ALJ to defer to "the reasonable findings of fact, reasonable interpretations of law, and reasonable application of fact to law by the Secretary."

The Secretary promulgated regulations implementing section 1869(f) at 42 C.F.R. Part 426. 68 Fed. Reg. 63,692. Section 426.110 defines the "reasonableness standard" as --

> the standard that an ALJ or the Board must apply when conducting an LCD or an NCD review. In determining whether LCDs or NCDs are valid, the adjudicator must uphold a challenged policy (or a provision or provisions of a challenged policy) if the findings of fact, interpretations of law, and applications of fact to law by the contractor or CMS are reasonable based on the LCD or NCD record and the relevant record developed before the ALJ or the Board.

The preamble to the implementing regulations states that this deference standard "recognizes the expertise of the contractors and CMS in the Medicare program--specifically, in the area of coverage requiring the exercise of clinical or scientific judgment." 68 Fed. Reg. at 63,703. The preamble goes on to state that --

> [s]o long as the outcome is one that could be reached by a rational person, based on the evidence in the record as a whole (including logical inferences drawn from that evidence), the [LCD] determination must be upheld. This is not simply based on the quantity of the evidence submitted, but also includes an evaluation of the persuasiveness of the material. If the contractor or CMS has a logical reason as to why some evidence is given more weight than other evidence, the ALJs and the Board may not overturn the determination simply because they would have accorded more weight to the evidence in support of coverage.

Id.

The regulations provide for the aggrieved parties to file a statement as to why the LCD is not valid (section 426.400(c)(5)) and copies of clinical or scientific evidence in support of the statement (section 426.400(c)(6)), for the federal party to file the LCD record (sections 426.418, 426.419), for an opportunity for the aggrieved parties to make a statement about the LCD record (section 426.425(a)) or submit additional evidence (section 426.403)), and for an opportunity for the federal party to respond (section 426.425(b)). Thereafter, the ALJ "applies the reasonableness standard to determine whether the LCD record is complete and adequate to support the validity of the LCD." 42 C.F.R. § 426.425(c)(1). "Issuance of a decision finding the record complete and adequate to support the validity of the LCD ends the [ALJ] review process." 42 C.F.R. § 426.425(c)(2).

Aggrieved parties have standing to challenge only the LCD provision that bars coverage of the treatment of which they claim to be in need. 42 C.F.R. § 426.110. Thus, as part of filling an acceptable complaint, an aggrieved party must submit a treating physician's statement that the aggrieved party needs the "service that is the subject of the LCD" provision. The ALJ's review is confined to "the provision(s) of the LCD raised in the aggrieved party's complaint." 42 C.F.R. § 426.431.

Before the ALJ, the aggrieved party "bears the burden of proof and the burden of persuasion for the issue(s) raised in the complaint." 42 C.F.R. § 426.330. The burden is "judged by a preponderance of the evidence." Id.

Aggrieved parties may appeal to the Board "any part of an ALJ's decision that . . . states that a provision of an LCD is valid under the reasonableness standard." 42 C.F.R. § 426.465(a)(1). The standard of review before the Board is "whether the ALJ decision contains any material error, including any failure to properly apply the reasonableness standard." 42 C.F.R. § 426.476(b).

"In applying the reasonableness standard to a provision . . . of an LCD, the ALJ must follow all applicable laws, regulations, rulings, and NCDs." 42 C.F.R. § 426.431(c); see also 1866ICPayday, DAB No. 2289, at 14 (stating "an ALJ is bound by applicable laws and regulations and may not invalidate either a law or regulation on any ground"); Sentinel Medical Laboratories, Inc., DAB No. 1762, at 9 (2001) (stating that it is "well established that administrative forums, such as this Board and the Department's ALJs, do not have the authority to ignore unambiguous statutes and regulations on the basis that

they are unconstitutional"), aff'd, Teitelbaum v. Health Care Financing Admin., No. 01-70236 (9th Cir. Mar. 15, 2002), reh'g denied, No. 01-70236 (9th Cir. May 22, 2002).

Therefore, the issue before the Board is whether the ALJ erred in concluding that the LCD record is complete and adequate to support the validity of the challenged provision under the reasonableness standard.

2. We find no material error in the ALJ's resolution on the merits.[7]

The core of the ALJ Decision consists of his review of the evidence relied on by the contractors as the medical and scientific basis supporting the LCD provision at issue and the opposing evidence proffered by the APs in an effort to show that the LCD record is not adequate or complete to support its validity. ALJ Decision at 40-57. We discuss the basis for the ALJ's conclusions briefly but do not repeat here his comprehensive review. We address in more detail the APs' allegations before us of error by the ALJ.[8]

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[7] We have fully considered all arguments raised by the APs on appeal and reviewed the full record, regardless of whether we have specifically addressed particular assertions or documents in this decision.

[8] In the appeal request, Dr. Calabrese discusses the scientific significance of articles which were submitted before the ALJ. She couches this discussion in many places as arising from her personal knowledge and expertise, and we consider these assertions that she makes as "the attending allergist-immunologist's position." See, e.g., AR at 101. The APs did not submit similarly detailed commentary on the exhibits to the ALJ, so, obviously, he had no opportunity to consider it. While the Board is not required to consider any argument or evidence that could have been but was not presented to the ALJ, we have considered Dr. Calabrese's comments here as arguments challenging the ALJ's understanding of and weighing of the evidence in the record before him, not as new evidence or arguments. As explained in our discussion, none of the comments demonstrates any error in the ALJ Decision.

A. Relative weight of scientific/medical evidence

In our consideration of the ALJ's evaluation of the record, we find useful guidance in section 13.7.1 of the Medicare Program Integrity Manual (MPIM), which advises contractors to "base" LCDs on "the strongest available evidence" and provides an order of preference to employ in assessing the relative weight of different kinds of evidence.[9] The following sources are identified in descending order of significance:

> **1. Published** authoritative evidence derived from **definitive randomized clinical trials** or other definitive studies, and
>
> **2. General acceptance by the medical community** (standard of practice), as supported by sound medical evidence based on:
>
> > a. **Scientific data or research studies** published in peer-reviewed medical journals;
> >
> > b. **Consensus of expert medical opinion** (i.e., recognized authorities in the field); or
> >
> > c. Medical opinion derived from consultations with **medical associations or other health care experts.**

MPIM § 13.7.1 (Rev. 71, 04-09-04). In order to conclude that the contractor could not reasonably determine that the use of TF therapy for the clinical conditions identified by the APs was not covered by Medicare, we would expect to see evidence of this caliber that contradicts the contractor's conclusions, i.e., definitive clinical studies[10] or, at least, general acceptance by the medical community founded on sound medical sources.

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[9] CMS did not mandate that the ALJ or the Board must use a specific hierarchy to evaluate evidence in LCD cases so we are not bound by this framework. 68 Fed. Reg. at 63,701. Nevertheless, we find the guidance to contractors in their preparation of LCDs helpful to us in considering the relative strength of the scientific research results on which the parties rely. While the ALJ did not expressly reference the manual language, his discussion reflects a similar understanding of the relative weight of different kinds of studies and of sources of medical opinion.

[10] In this context, we use "clinical studies" in reference

(Continued . . .)

Under the reasonableness standard, furthermore, an LCD record is not shown to be incomplete or inadequate merely because the contrary evidence submitted to the ALJ could support a different conclusion than that reached by the contractor based on the LCD which it developed. The evidence on the record before the ALJ must show that the contractor could not reasonably have reached the conclusion it did if the evidence as a whole had been considered. If the contractor could still reasonably reach the conclusion it did, neither the ALJ nor the Board will substitute an alternative conclusion, even were we to consider an alternative also reasonable and even preferable.

In other words, it is not sufficient to show that additional evidence exists that was not included in the record on which the contractor based the LCD. It is necessary, rather, for the APs to show that that additional evidence makes a difference, and that it does so to such a degree as to make the conclusions on which the LCD is based unreasonable.

B. ALJ review of the basis for the noncoverage LCD

The ALJ reviewed the basis set out by Palmetto for adopting the LCD, which in turn relied on the literature review and other research conducted by NHIC. ALJ Decision at 43-50, discussing CMS Ex. 22 (Third LCD). The essence of that basis was that the research literature did not contain any clinical study definitive enough to demonstrate that TF therapy had been proven to be a safe and effective treatment. Id. at 50.

While some studies showed positive or at least promising results for various uses of TF in relation to many different conditions, the ALJ found that the contractor could reasonably consider those studies not sufficiently definitive because most involved single case reports or small groups, lacked meaningful controls, or were contradicted by other reports that found no clinical benefits.[11] Id. at 43-50. The contractor also considered

(Continued . . .)

to scientific research involving human patients.

[11] Although the LCD record produced by CMS before the ALJ did not include the articles which Dr. Calabrese submitted to the ALJ as exhibits in support of the APs' position, it is not disputed that articles that she has relied on as establishing

(Continued . . .)

medical textbooks, contacted leading university experts in immunology and looked at other insurers' practices without finding any evidence that TF therapy had achieved general acceptance in the medical community. Id.

We note that Dr. Calabrese asserts that she was previously reimbursed for TF therapy claims by the contractor predating NHIC. See, e.g., AR at 10; 50. She has not, however, provided a single example of a claim which disclosed that it was for TF therapy and which was paid by the prior contractor. Even if the APs had been able to produce evidence that a contractor had paid for TF therapy at some point, such evidence would not alone suffice to show general medical acceptance.

The ALJ arrived at the following summary based on his discussion of the methodology and results of the studies submitted with the LCD record:

> The patient studies are enlightening regarding clinical investigation of TF but show that TF therapy has raised more questions than were answered. Where certain patient studies indicated that TF might have played a role in easing symptoms or the progression of disease, it is clear that researchers remained cautious about making any conclusive pronouncements as to its efficacy.
>
> None of the patient studies discussed in the articles or papers submitted by CMS involved patients receiving TF therapy for the clinical indications Dr. Calabrese seeks to treat - allergies, including allergic hypersensitivity to chemicals, and abnormal cell-mediated immunity/delayed type hypersensitivity. The absence of evidence of studies showing the efficacy of TF for allergies, including allergic hypersensitivity to chemicals, and abnormal cell-mediated immunity/delayed type hypersensitivity, is consistent with the Palmetto and CMS position that TF has

(Continued . . .)

the efficacy of TF therapy were before the contractor when the LCD at issue was developed and were not included in the LCD record CMS submitted to the ALJ to avoid duplication. ALJ Decision at 44; Memorandum Regarding Non-Existence of LCD dated March 1, 2008, at 3-4 (item 29 in CRD record index).

> not been shown to be efficacious or safe and effective for those diagnoses.

ALJ Decision at 50.

The ALJ recognized, however, that his analysis did not stop with determining that the record as it was developed by the contractor could reasonably support the contractors' conclusion of noncoverage. Id. He therefore also considered whether the material submitted by the APs demonstrated that the LCD record before him was not complete or adequate to show that the contractor could reasonably reach that conclusion. Id. at 50-57. The ALJ reviewed all of the 304 articles and letters from scientific and medical journals and extracts from textbooks submitted in opposition to the LCD provision and concluded they did not establish that the record was not complete and adequate to support the validity of the LCD. Id. at 50.

The APs allege repeatedly that the ALJ failed to understand the scientific merit of the articles and failed to give their evidence appropriate weight. We review these arguments and the ALJ's conclusions to determine if the APs have shown that they contain material error. We turn next, therefore, to the APs' arguments on appeal.

> C. Relevance of research studies to the use of TF which the APs contend should be covered

In considering the variety of scientific articles and medical opinion proffered by the APs, we note that the degree to which particular research is relevant to and supportive of the APs' challenge to the LCD provision of noncoverage of TF therapy depends in part on how closely the protocol and patients involved resemble the kind of therapy that the APs argue should be entitled to coverage. As explained earlier, all of the APs are diagnosed with cell-mediated immunoregulatory defects which manifest in a variety of symptoms. AR at 2, 104, 126, 173-74. Therefore, the most relevant evidence is that which addresses the use of TF therapy to treat this condition.

The literature presented by the APs covers many different kinds of TF preparations.[12] In many studies, some of them discussed

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[12] Our discussion of the scientific exhibits proffered by the APs is hampered by several factors. As the ALJ noted, the

(Continued . . .)

below, donors either were tested for sensitivity to a particular antigen or were intentionally exposed to a particular antigen. The TF prepared from their blood was then introduced into naïve recipients (i.e., those not previously reactive to or exposed to the antigen).[13] Such TF was used to try to transfer antigen-specific responses to the recipient. Dr. Calabrese instead uses TF from pooled blood of donors not specially selected or treated in order to provide "non-specific immunomodulatory treatment." AR at 104. The most relevant scientific and medical evidence, therefore, would be research using pooled donor blood without

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(Continued . . .)

AP exhibits were not properly marked when submitted. ALJ Decision at 6 n.4. Even now that they are marked, they are difficult to review on appeal for multiple reasons. For example, a single exhibit number sometimes contains numerous articles and the exhibit contents are not numbered consecutively. We therefore use the original page numbers of the journal articles. In addition, some exhibits are not accurately described in the APs' exhibit index submitted by the APs, as the ALJ noted in regard to AP Exhibit 3. Id. (The absence of the material cited in the index for AP Exhibit 3 is striking because it purported to be one of the very few articles dating post-2000 to deal with TF therapy in humans.) Furthermore, some of the book chapters identified in the index are not actually present in the corresponding exhibits, which contain only the frontal material from the book. See, e.g., AP Exs. 5-7. Finally, Dr. Calabrese frequently fails, in commenting on the numerous scientific articles and chapters on which the APs rely, to distinguish language taken verbatim from the cited material from her own observations or commentary and fails to identify the articles by their exhibit numbers. Compare, e.g., AR at 232 with J. Byston et al., Effect of Anti-Herpes Specific Transfer Factor, 9 Biotherapy 73 (1996)(A.P. Ex. 24).

[13] For example, many studies submitted by the APs support the hypothesis that, when TF therapy has shown some benefit, the results were based on the transfer of antigen-specific reactivity from a donor exposed to the antigen rather on "nonspecific immunostimulation." Littman, B.H., et al., Transfer factor treatment of chronic mucocutaneous candidiasis: Requirement for donor reactivity to Candida antigen, 9 Clinical Immunology and Immunopathology 97 (1978) (A.P. Ex. 74).

prior sensitization of the donors to a particular antigen and evaluating the immunomodulatory benefits.

The literature also reflects debate about how non-antigen specific TF might benefit recipients. Some argue that TF may stimulate immune response to many different antigens, while others argue that TF may contain many elements that improve the overall functioning of an impaired immune system without connection to any particular antigens. Dr. Alan S. Levin, one of the APs' expert witnesses, has supported the latter position in some of his writing. Thus, he reported in a chapter on the use of TF therapy with food allergies that TF included a "mix of immunopotentiators" including dozens of active components. Levin, A., "Chapter 60: Transfer Factor and Allergies," in Brostoff, J. and Challacombe, S.J., Food Allergy and Intolerance at 995 (1989) (A.P. Ex. 2); AR at 172. Some of these "moieties" offered the possibility of immunomodulation, i.e., improving the functioning of a patient's immune system generally rather than merely improving the patient's ability to respond to one allergen or pathogen. Some moieties, according to Dr. Levin, were able to reestablish an overall ability to suppress the body's overreaction to harmless agents in the environment or in the body itself (auto-immunity). A.P. Ex. 2, at 997.[14] Dr. Calabrese, however, appears to support the first theory, contending that TF is not currently considered to serve as an "adjuvant" or booster to the existing immune response of recipients. AR at 204-05. She asserts that her method of pooling blood products from multiple donors maximizes the variety of antigen-specific factors. Id. Therefore, again, the most relevant research would be that which supported the APs' claims that TF therapy can serve to enhance the cell-mediated response to many different antigens rather than research showing only a general adjuvant effect on the functioning of the immune system.

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[14] We also observe that, although Dr. Levin concluded in his chapter that TF therapy "may be a helpful adjunct to the management of otherwise refractory food and inhalant allergy patients," he also reported adverse side effects in 5% of patients and no improvement in 19% and noted the concern about blood-born diseases (although asserting that no viral illness transmitted by TF had been reported). A.P. Ex. 2, at 1001.

Finally, we note that research identifying a plausible and effective biological mechanism for the asserted actions of TF would be relevant. In a signed statement dated January 7, 2008, however, Dr. Levin acknowledges that the molecules that may cause the transfer of functionality have still have not been clearly characterized, other than that they are small-sized (likely 5,000 Daltons or less in molecular weight) and apparently have some ability to respond specifically to particular antigens or parts of antigens. See A.P. Ex. 184, at 3-4. Dr. Levin's textbook chapter states that the theory that such small fragments from disrupted white blood cells could effect a transfer of delayed-type hypersensitivity was met with "a great deal of resistance" from immunologists. A.P. Ex. 2, at 995. The capacity of antibodies to react with specificity to an enormous diversity of substances has been explained through identifying genetic mechanisms, but no such biological explanation has been identified for TF. Dr. Levin suggests that "it is possible that [TFs] operate through an unique mechanism of antigen presentation and T-cell activation" that somehow transfers certain cell-mediated immune responses without affecting B cell-mediated functions. A.P. Ex. 184, at 4.

Thus, the ALJ correctly stated that the record indicates that even proponents of TF therapy, such as Dr. Levin and others, agree that no plausible mechanism of action has so far been elucidated, that the relevant molecules have not been isolated, and that numerous questions about TF remain unanswered. ALJ Decision at 45-48; see, e.g., J. Dwyer, Transfer factor in the age of molecular biology: A review, 9 Biotherapy 7-11 (1996) (A.P. Ex. 36). Dr. Calabrese herself does not deny this uncertainty about what TF is or how it works.[15] While Dr. Calabrese correctly points out that some treatments, such as aspirin or penicillin, became widely accepted prior to any full elucidation of how their effects were achieved (AR at 206, 230, 261), the absence of a demonstrable biological explanation makes

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[15] Dr. Calabrese does point to work by Dr. Charles Kirkpatrick suggesting that the "one of the most potent moieties in TF" is gamma interferon. AR at 102. Gamma interferon is a cytokine and Dr. Calabrese notes that considerable work has been done in recent years in identifying and tracing the signaling behavior of numerous cytokines. Id. She does not, however, suggest that TF consists simply of gamma interferon or that inclusion of cytokines as possible elements of TF explains why, in her view, it may act against multiple antigens.

Furthermore, the APs note that Dr. Levin, who provided a declaration in their behalf, served on the California Medical Board allergy-immunology panel in the 1980s and early 1990s. AR at 171; A.P. Ex. 184; see also Motion for Expedited Hearing at 67 (item 60 in CRD record index). He is identified throughout the record as an early and prominent proponent of TF therapy. Notably, however, Dr. Levin makes no statement in his declaration about any approval or regulation of TF therapy by that Board. A.P. Ex. 184.

Moreover, CMS presented evidence that, in a proceeding concerning Medicare reimbursement to Dr. Calabrese for TF therapy, a California allergist who does not support the efficacy of TF therapy stated that the California Medical Board "did not certify [Dr. Calabrese's] treatment protocol as [Dr. Calabrese] contends since the [Board] does not have a protocol certification function." CMS Ex. 1, at 16. Thus, contrary to what the appeal request suggests, CMS provided evidence contradicting the assertion that TF therapy was approved. Her statement that patients "can have confidence in the Medical Board of California as having investigated and approve[d] [TF] immunomodulatory regulatory agent for their clinical significant underlying Th1-Th2 immunoregulatory defect" (AR at 231) is insufficient because it lacks any corroborating support in this record even though it was contradicted by the cited statement.

As this analysis indicates, it is impossible to directly answer a question about what CMS policy authorized the ALJ to make a suggestion about Dr. Calabrese's mental capacity since the ALJ never made such a suggestion. Nor can we rely on the premise inherent in the question, i.e., that the ALJ made the alleged suggestion in the process of rejecting Dr. Calabrese's supposedly undisputed assertion about the Medical Board's approval. To the contrary, that assertion was in dispute and lacks record support.

Similarly, as to many of the scientific articles provided in the APs' exhibits, the appeal request repeatedly asks, "what law or other proven evidence" gave the ALJ authority to "exclude the materially relevant clinical/scientific facts" in each cited article and to exclude testimony about the article by Dr. Calabrese who was qualified to explain the "basic science, differential diagnosis, pathophysiology, treatment implications and importance" for these patients. See, e.g., AR at 227. Again, this misrepresents the ALJ's action. He did not exclude any of the scientific evidence proffered by the APs, but rather reviewed it and concluded that it did not suffice to make the

more crucial the need for definitive scientific proof of safety and effectiveness or, at least, for broad acceptance in the medical community.

D. APs' challenges to the ALJ's review of scientific merit of TF therapy - preliminary difficulties

We note that the form of the APs' appeal to us presents obstacles to discerning and addressing the APs' specific legal or evidentiary arguments. The appeal couches its challenges to the ALJ Decision largely in the form of numerous questions asking what CMS policy or other law gave the ALJ the authority to take various actions or reach various conclusions. See AR passim. These questions are problematic in that they often attribute to the ALJ actions or conclusions which the record demonstrates he did not take or assert. They also assume or assert that allegations made on behalf of the APs are uncontested or proven when the record does not support those assumptions or assertions. Id. One question posed in the appeal request illustrates these difficulties:

> The 11 Appellants ask the DHHS DAB what CMS policy allows Judge Keith Sickendick, an independent trier of fact, to suggest that the attending allergist immunologist is so impaired that she does not know from her own contact working directly with the Medical Board of California that human dialyzable leukocyte extract, the transfer factor immunomodularity therapy, has been approved and regulated by the Medical Board of California for decades for our class of Medicare patient when that has been [an] uncontested fact in the record since 2003?

AR at 52. The ALJ Decision nowhere suggests any impairment on the part of Dr. Calabrese. As to the California Medical Board, Dr. Calabrese acknowledges that her treatment regimen represents a minority opinion among allergist-immunologists but does assert to us that the California Medical Board "has been extremely complimentary to me regarding the preservative free antigen immunotherapy and transfer factor immunomodulatory therapy program" and has "stated that my protocols are the ones that are used for the state." AR at 104; see also AR at 17, 52, 60, 257. She does not, however, provide any documentation of these alleged comments and statements by the California Medical Board or any other evidence of approval of her use of TF therapy by any professional group. Yet, if the California Medical Board officially investigated, approved, and regulated TF therapy, one would expect there to be some written record of such activity.

record inadequate to support the validity of the LCD. The APs submitted declarations by other physicians, as well as Dr. Calabrese's own declarations and statements. In accordance with the statute and regulation, once the ALJ determined that the record before him was complete and adequate to support the validity of the LCD under the reasonableness standard, the ALJ did not proceed to discovery and the taking of evidence at a hearing. While Dr. Calabrese therefore did not have the opportunity to provide in-person testimony, this outcome cannot fairly be characterized as an exclusion of her explanations or a rejection of her qualifications. Furthermore, the ALJ considered the opinions expressed by Dr. Calabrese in her various filings (rather than limiting her role to that of the usual party representative) and found her opinions "weighty." ALJ Decision at 42. He simply did not find them sufficient to "outweigh the other evidence of record that supports the validity of the LCD." Id. Again, the question as framed in the appeal request is based on erroneous assumptions about what the ALJ did.

We therefore do not attempt to discuss individually each of the many questions or comments of this nature in the appeal request (although we have considered each in arriving at our analysis). Instead, we seek to discern the underlying arguments that the APs put forward as to why the ALJ should have found their evidence sufficient. We focus here on those arguments that allege error in or lack of supporting evidence for the ALJ's ultimate conclusion on the scientific merits.

E. APs' challenges to ALJ review of scientific merit of TF therapy - arguments that the ALJ did not give sufficient weight to certain evidence

i. Section 1879 and individual physician knowledge

Dr. Calabrese argues that her prescription of TF therapy should have been enough in itself to establish that the therapy was covered because "Section 1879 of the [Act] states that a physician knows by virtue of their license[] to practice medicine whether care isn't reasonably and medically necessary." AR at 33; see also id. at 53. Section 1879 does not contain such a statement and nowhere guarantees that every item or service provided by a licensed physician will be covered by Medicare. That section simply allows payment to be made for items or services, even though they may not be covered under the medical necessity requirements, where the provider neither knew nor could reasonably have been expected to know that payment

would not be made. One function of an LCD is to provide advance notice of such noncoverage to all providers in a contractor's area, which would make payments to them under section 1879 unavailable. See MPIM § 13.13 (stating "[c]ontractors publish LCDs to provide guidance to the public and the medical communities within their jurisdictions").

The fact that a single provider believes that an item or service is medically reasonable and necessary for patients is not a sufficient basis to demonstrate that an LCD providing that that item or service is not covered by Medicare is not valid. The MPIM specifically notes that "acceptance by individual health care providers, or even a limited group of health care providers, normally does not indicate general acceptance by the medical community." MPIM § 13.7.1. While the judgment of and documentation by an attending physician play an important role in care delivery to individual patients, contractor-wide LCDs are founded on evaluating the best scientific and medical sources under evidence-based standards to ensure that Medicare pays only for care that is medically reasonable and necessary. MPIM § 13.7.1.

ii. Statements of the APs' experts

The APs also rely on declarations from three other physicians: Dr. Levin, Dr. Douglas H. Sandberg, and Dr. Gerald H. Ross. The ALJ did not give significant weight to these declarations because, although each physician opined that TF therapy could be safe and effective for certain allergy patients, none of them cited to any published studies involving the use of TF to treat such patients.[16] ALJ Decision at 57.

The APs assert that these physicians' statements should have been sufficient to establish medical acceptance of TF therapy.

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[16] As to these physicians, the ALJ noted, correctly, that the APs' repeated references to them as "Daubert-qualified" only indicate that they have been permitted to testify and provide expert opinions in federal court cases. ALJ Decision at 57. They were similarly permitted to provide opinions in their declarations before the ALJ. The ALJ was not obliged, however, to accept their opinions in the face of the scientific evidence in the record in support of the contractor's conclusions in the LCD simply because the physicians are "Daubert-qualified."

AR at 104. As discussed below, we conclude that the ALJ did not err in his treatment of these experts.

The APs point first to Dr. Levin's statement. AR at 104-10, citing A.P. Ex. 184. Dr. Levin opines that, for a small set of patients presenting with extensive allergies, an underlying disease process cannot be discovered even after extensive medical evaluation, and that, for such patients, "specific and non-specific immunomodulatory treatment is warranted," including TF therapy and IV gammaglobulin. A.P. Ex. 184, at 1.

Dr. Levin cites three sources for his position that TF "has been shown to restore cell mediated immunity to immunodeficient patients with opportunistic infections": (1) a 1983 study by Steele et al. reporting high success rates using specific TF from chickenpox immune donors to prevent chickenpox in children with leukemia; (2) a 1983 report of eleven patients treated with TF from donors immune to herpes simplex who showed reduction in persistent or recurrent herpes infections; and (3) a textbook chapter from Principles of Internal Medicine on polyglandular autoimmune syndrome. Id. at 5. None of these studies correlates to Dr. Calabrese's particular use of TF therapy. The first two studies, both more than 25 years old, deal with the use of TF from donors sensitized to a particular antigen (i.e. chicken pox or herpes simplex virus) to transfer immunological response to that antigen to other patients not capable of effective reactivity to that antigen. The TF therapy described by Dr. Calabrese, by contrast, uses pooled blood from healthy donors without known specific immunities and does not seek to boost response to a single target antigen in the recipient. AR at 104. The chapter excerpt on polyglandular syndrome on which Dr. Levin relies notes that symptoms include candidiasis and asserts that "partial remission has been reported with a combination of ketoconazole [an anti-fungal medicine] and transfer factor." A.P. Ex. 4, at 1812. Dr. Calabrese does not assert that the APs have polyglandular autoimmune syndrome. Furthermore, this brief reference does not cite specific studies and does not establish that TF, without accompanying conventional treatment, is an accepted modality for polyglandular syndrome.

Dr. Levin also asserts that TF "has been shown in many studies to be efficacious in a number of immunodeficiency disorders" involving persistent infections of many kinds, but does not cite any such studies. A.P. Ex. 184, at 5. Finally, he cites three studies as showing increased survival time and remissions in cancer patients. Id. Only one of those studies dates from

after 1980 and the relevance of those studies to the clinical conditions of the APs here (who are not identified as cancer patients) and their treatment with TF is neither clear on the face of those studies nor explained by Dr. Levin. Therefore, the ALJ did not err in concluding that none of the authorities relied on by Dr. Levin, viewed alone or with other evidence in the record, provides adequate support for the APs' position that the basis for the LCD was unreasonable.

The APs' second expert, Dr. Sandberg, states that he treated Dr. Calabrese's son with TF therapy and referred another patient to Dr. Calabrese for continued treatment with TF after Dr. Sandberg retired. A.P. Ex. 184, at 8. He opines that "Medicare should not preclude reimbursement for these safe and effective immunotherapies because they are self-administered." Id. (emphasis added). Dr. Sandberg offers no authorities to support his characterization of TF therapy as "safe and effective." Moreover, self-administration is not the basis for the noncoverage provision in the LCD, and, therefore, this portion of Dr. Sandburg's statement is not relevant here.[17]

Finally, Dr. Ross's statement is also inadequate to show that TF therapy is now generally accepted in the medical community. In fact, it demonstrates the opposite. Dr. Ross admits that it "is fair to say that those physicians who use preservative-free antigen immunotherapy and transfer factor among allergist-immunologists would be within a minority of that group." A.P. Ex. 185, at 3. He notes that Dr. Calabrese's practice is "unique," since the most experienced physicians who provided this treatment have retired. Id. at 4. Dr. Ross argues that the fact that the majority of the relevant medical community does not use this treatment should not logically demonstrate a lack of legitimacy or efficacy, using the analogy that only a small group of neurosurgeons may perform a certain life-saving procedure because those doctors may the only ones with the expertise or the cases may be rare and complex. Id. at 3-4.

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[17] In 2003, NHIC questioned individual claims submitted by Dr. Calabrese for multiple other reasons including Medicare restrictions on payment for self-administration of injected treatments, inadequate documentation, and lack of FDA approval of TF as a drug or biological. CMS Ex. 1. We do not review these reasons since the issue before us is limited to the medical necessity policy reflected in the LCD.

Dr. Ross is logically correct that the mere fact that a small subset of physicians perform a particular procedure does not per se prove that the procedure is illegitimate. Where a procedure is rarely performed, either because few doctors are capable of performing it or few patients require it, its efficacy may nevertheless be well-accepted in the medical community at large and may be well-supported in the medical literature. The APs, however, have failed to demonstrate that either condition exists as to the therapy they receive with TF.[18]

iii. Longstanding use and orphan population

The APs contend that the ALJ upheld noncoverage of TF therapy merely because it "was developed in 1955 and is only used in a tiny orphan population." AR at 98. Neither fact, however, is the basis for the ALJ's conclusion. The point that the ALJ makes about the age of the vast majority of articles which arguably support various uses of TF as therapy is not that TF was first developed so long ago but that the absence of recent work supporting any current use for TF is consistent with the contractors' conclusion that TF's early promise as therapy failed to bear fruit. ALJ Decision at 45-50. Although Dr. Calabrese decries what she calls the tendency to "marvel at what is shiny and new - stem cell therapy, nanomedicine, engineering advances in robotics, and so forth" (AR at 206), she does not establish that such novel approaches are covered by Medicare unless they can be shown to be safe and effective for clinical use. In short, the question is not whether a treatment is old or new, but whether it is medically necessary based on evidence of appropriate weight.

Further, the ALJ did not deny that a treatment may be shown to be safe and effective for use in a specific orphan population.

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[18] Dr. Ross also argues that there is not and should not be any requirement that "every therapeutic modality must be approved as 'eligible,' in order to be used to treat a certain medical diagnosis . . . ." A.P. Ex. 185, at 5. CMS has not taken the position that every treatment for every condition must be approved as eligible to be covered. Instead, both the Act and CMS regulations and policy simply permit contractors to develop policies on whether and when specific treatments will or will not be covered based on evidence as to their medical necessity for particular conditions.

He found, instead, that the APs had not demonstrated that this treatment had actually been shown to be safe and effective "for the treatment of allergies, including allergic hypersensitivity to chemicals, and abnormal cell-mediated immunity/delayed type hypersensitivity or any other diagnosis," at least not by a quantum of evidence necessary to find the contractors' contrary conclusion as reasonable. ALJ Decision at 50.

Dr. Ross also asserts in his statement that TF therapy is appropriate and necessary in complex cases of selected patients with both abnormal cell-mediated immunity and extensive allergies who are unresponsive to more commonly-used treatment (the group on which Dr. Calabrese focuses) based on "a long history of safe and successful use" in such cases. A.P. Ex. 185, at 6. Dr. Ross appears to base his assessment that this use of TF therapy has been "safe and successful" solely on his own practice prior to his retirement, on Dr. Calabrese's experience, and on the research and practice of three prominent early proponents of TF therapy, i.e., Drs. Levin, Kirkpatrick, and H. Sherwood Lawrence. Id. at 2, 5-6. As noted before, even if we accept Dr. Ross's assertion about the experience of these physicians with their patients, the experience of a handful of practitioners does not suffice to prove general medical acceptance.

Notably, one of the more current (1996) studies submitted by the APs sums up the "hope for the future" for TF therapy, even after all the years of pilot studies and exploratory research, as lying in the need for --

> clinical trials with known amounts and dosages of pure standardized materials, of known composition and predictable effects available in adequate quantities for complete courses of therapy, and tailored to meet not only the needs of the specific patient, but also to selectively cope with the demands of the specific disease.

Lawrence, H.S. and Borkowsky, W., Transfer factor - current status and future prospects, 9 Biotherapy 1, 4 (1996) (A.P. Ex. 71). Our review of the complete record demonstrates no error in the ALJ's overall conclusion that the APs have not documented the realization of this hope.

iv. Animal studies and general studies of pollution exposure

In weighing the voluminous scientific articles offered by the APs, the ALJ first correctly determined that certain categories of studies were not entitled to significant weight or not relevant as evidence of the efficacy of TF therapy for the clinical conditions at issue. ALJ Decision at 51-52. These categories included animal studies and environmental pollutant exposure studies. Id.

The ALJ found that the laboratory studies with mice and other animals were an "insufficient basis for finding TF to be an effective, reasonable, or necessary treatment for humans." ALJ Decision at 51. Dr. Calabrese indeed acknowledges that studies "in rodents are not automatically good correlates for humans," and that TF studies in guinea pigs, for example, did not track the action of TF in humans. AR at 154. She nevertheless points to recent (2008) work in mice as showing strong correlation in the TH1 and TH2 cytokine responses in humans and mice. AR at 154-55. This work explores only the comparative functioning of the immune systems of mice and humans and does not address how either responds to TF.

The APs do point to a 1974 study in which mice demonstrated transferred reactivity to a chemical after TF injection, and suggest that mice are a better model than guinea pigs to test the effects of TF. AR at 156-57. It may be reasonable to suppose that species whose immune systems resemble humans in the aspect of interest (here, TH1 and TH2 cytokine immunobiology in mice) are likely to serve as better models for testing the response of those systems to TF than those species whose immune systems do not (such as guinea pigs). It does not follow, however, that experimentation in animal models can suffice to compel coverage of TF therapy in humans absent rigorous clinical follow-up studies or appropriate evidence of general acceptance in the medical community.

The APs also point to studies using mice to test whether the action of human TF is antigen-specific. See, e.g., AR at 212; A.P. Ex. 20. Dr. Calabrese argues, as a matter of science, such research with mouse models is "critical" to avoid use of the Medicare participant "as a research subject." AR at 212-13. Dr. Calabrese is certainly correct that human subject research has "inherent ethical limitations" and that animal studies may be important to provide preliminary support for future clinical research. AR at 213. Again, however, this argument does not

make such laboratory research always a good correlate for human studies (as Dr. Calabrese herself acknowledged), much less an acceptable substitute for clinical studies or direct evidence of medical necessity.

We conclude, therefore, that the APs' arguments are not a basis for rejecting the ALJ's conclusion that these animal studies, by themselves or with other evidence, do not demonstrate that the record is incomplete or inadequate to support the validity of the LCD.

The APs also challenge the ALJ's refusal to rely on reports submitted by the APs on the effects of diesel exhaust particles (DEP) contained in polluted air on the immune systems of animals and human volunteers (ALJ Decision at 51, citing AP Exs. 153-179). AR at 405-33. The studies report on effects of DEP exposure on airway inflammation and asthma, cytokine expression and T cell changes, but do not demonstrate any particular role of TF in response to DEP exposure.

These studies, like many of the animal models and in vitro experiments seeking to elucidate immune system functioning, constitute basic science which may underlie an eventual clinical application. They do not, however, in themselves definitively establish that a clinical application is safe and effective for use in patients. A large number of studies included in the APs' exhibits represent such experimental laboratory efforts to identify the nature of TF molecules or to clarify their chemical activity. See, e.g., AP Exs. 16, 20-22. The absence of a definable mechanism of action may present a problem for general acceptance of a putative treatment, but basic research in pursuit of such a mechanism is not in itself sufficient to establish clinical relevance.

This point is articulated in the very articles highlighted in the appeal request. For example, one researcher commented that the activity of TF in the laboratory and in the clinic appear distinct and that additional experiments "which show correlation between in vivo transfer activity and in vitro effects are required to establish any direct relationship." D. Burger, et al., Human transfer factor: Effects on lymphocyte transformation, 117 Journal of Immunology 782, 787 (1976) (A.P. Ex. 22).[19] The laboratory studies in the AP exhibits are thus

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[19] In this context, "in vivo" refers to the activity shown

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not a sufficient basis to conclude that the use of TF has been definitively shown to be medically necessary for any specific condition or that its use has gained general acceptance in the medical community.

v. Patient reports involving individual cases or different clinical conditions

The ALJ pointed out that many other studies submitted by the APs involve the use of TF with patients whose clinical conditions differ from that of the APs and/or constitute "anecdotal" reports of individual cases. ALJ Decision at 51-52, 55-56. Dr. Calabrese suggests that the ALJ was misled into thinking that the literature on TF therapy "is so without academic rigor that it purports treatment for dozens of different diseases" because he lacked her expert understanding of the literature. AR at 102. She does not deny that, as the ALJ reported, the literature contains reports of research on the effectiveness of TF therapy in treating patients presenting with numerous different conditions, including "atopic dermatitis, Hodgkin's disease, chronic mucocutaneous candidiasis, herpes simplex, Epstein-Barr virus/cytomegalovirus infection, Wiskott-Aldrich syndrome, asthma associated with frequent infections, infection and malnutrition in children, leprosy, chronic active Type B hepatitis, multiple sclerosis, leukemia patients with susceptibility to varicella-zoster infection, cutaneous

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(Continued . . .)

by TF in living organisms, as opposed to its activity in laboratory experiments or test tubes which are "in vitro." Dr. Calabrese suggests that Burger's claim of inconsistency between the two was overcome by Dr. Kirkpatrick's work on gamma interferon in the late 1980s which she described as showing the "in vivo and in vitro literature fit like a lock and key." AR at 228. We need not resolve whether Dr. Kirkpatrick's work shows that there is no inconsistency in the observed activity of TF in the laboratory and the clinic. Our only point here is that the absence of rigorous and relevant in vivo clinical studies establishing that TF therapy is safe and effective for the particular clinical conditions at issue supports the reasonableness of the noncoverage determination. In vitro laboratory research may help elucidate the mechanisms by which TF acts but cannot suffice to establish that TF therapy is medically reasonable and necessary for a particular condition.

leishmaniasis, Behcet's syndrome, and cancer." ALJ Decision at 48, citing CMS Ex. 8 (H. Hugh Fudenberg, M.D. and H. Haskell Fudenberg, *Transfer Factor: Past, Present and Future*, 29 Annual Rev. Pharmacol. Toxicol., 475, 489-99 (1989). Instead, Dr. Calabrese argues that patients with these diseases do not respond to TF therapy unless they also have abnormal cell-mediated immunity. AR at 102. She emphasizes her ability to differentially diagnose those patients with, for example, asthma or multiple chemical allergies who will respond to TF therapy because of their comorbidity with abnormal cell-mediated immunity. Id. at 102-03.[20]

The difficulty with this argument is that the vast majority of studies testing TF formulations with patients suffering from these diseases do not distinguish which patients also had demonstrated abnormal cell-mediated immunity or assess how the responses of those patients to TF differed. Dr. Calabrese asserts that, while the results in these TF studies were, as the ALJ states, "mixed," the results in the subset of patients who are like those whom she treats are "extremely impressive." AR at 102. She then asserts that this conclusion is reflected "throughout the single and double blind placebo controlled studies included in the clinical and scientific citations." Id. She does not, however, specifically identify any single or double blind placebo controlled studies distinguishing patients whose disease states involved abnormal cell-mediated immunity from those who did not have that additional condition and assessing the groups' differential responses to TF therapy.

The ALJ did identify and discuss in detail one study in which 50 chemically sensitive patients were divided into four categories based on the normality or abnormality of their T and B

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[20] The ALJ stated that Dr. Calabrese emphasized in a declaration before him that she "does not treat patients with Multiple Chemical Sensitivity Syndrome, contrary to past statements of NHIC staff and the Board in DAB No. 2050, at 4." ALJ Decision at 42 n.26. In fact, Dr. Calabrese at various times has referred to patients having multiple or extensive chemical sensitivities and allergies, but, as noted above, her assertion is that she is not treating them with TF for that condition directly as opposed to treating them for underlying immune conditions which may be implicated in their sensitivities.

lymphocyte status and their cell-mediated immunity and then treated for varying periods of time with TF. ALJ Decision at 52-55, discussing A.P. Ex. 211, at 5-20 (J. Rea, M.D., 4 Chemical Sensitivity 2721-42 (1997)). Overall, the authors reported that 78% of the patients had some improvement in some parameters tested, while 22% had none and, and in some cases either worsened or had to stop therapy because of side effects. The ALJ reasonably discounted this study because no control group was used to compare the clinical course of similar patients not taking TF and because many of the patients were reported to have used other immunotherapy and to have made environmental changes at the same time. ALJ Decision at 54-55. We also note that the patients with normal numbers of lymphocytes and abnormal cell-mediated immunity showed slightly lower response rates than those patients who were normal on both measures at the start of the trial. A.P. Ex. 211. This result actually appears inconsistent with Dr. Calabrese's position that a patient's positive response to TF therapy depends on whether the patient has abnormal cell-mediated immunity. She argues nonetheless that "even in this group, the therapy was successful in 50% of the patients," which she calls "dramatic." AR at 233. Since this study had no controls, however, it is not possible to discern from this study whether the patients would have done better or worse without TF therapy or whether any improvement was attributable to the other changes in their treatment and environment rather than to TF therapy.

Dr. Calabrese's summaries of clinical studies also treat as confirmatory any evidence that use of TF altered the recipient's response to an antigen, such as converting skin tests from negative to positive. For example, she points out that 13 of 14 patients with immunodeficiencies who received TF injections in one study showed at least some newly positive test result. AR at 272-73, citing C. Griscelli, Transfer factor therapy in immuno-deficiencies, 18 Biomedicine 18 (1973) (A.P. Ex. 51). However, she omits the study findings that "[c]linical improvement was observed in only 2 cases of Wiskott-Aldrich," and that "[t]herapeutic effects were absent or uncertain in the other cases." A.P. Ex. 51, at 18. The LCD is not based on a conclusion that injections of TF have no effects at all on the results of allergy tests. Studies that report or test for such effects, while scientifically interesting, are not sufficient to establish that, contrary to the findings supporting the LCD, TF therapy serves a well-documented or well-accepted clinical role in producing therapeutic response in particular clinical conditions.

In sum, the studies of patients with a variety of diseases do not provide a basis for disregarding other studies (showing little or no benefit from TF therapy) merely because one possible reason why some study patients failed to benefit was that they did not have concomitant abnormal cell-mediated immunity.

Dr. Calabrese opines that the ALJ failed to recognize the "extreme value of single case reports," in light of the fact that all her patients are "outliers" with "more than one underlying pathophysiology, more than one diagnosis, . . . polysymptomatic, and . . . with different patterns of symptom relief over time." AR at 208. She argues that there "will be no double-blind placebo-controlled studies" in patients whose cases "lie outside the usual spectrum of illness." AR at 243. Neither the ALJ nor we have suggested that reports of the course of treatment or illness in individual patients are meaningless or devoid of medical interest. While double-blind placebo-controlled studies are generally considered the gold standard of authoritative clinical studies, they are not the sole basis on which a determination of medical necessity may be supported. As the MPIM explains, general acceptance in the medical community may be sufficient if it has scientific support. However, the ALJ properly found that the record showed neither general acceptance nor adequate scientific support in this case.

Dr. Calabrese also suggests that the LCD somehow forces doctors in the Medicare program "not to elaborate on the unique characteristics of the individual single case report" or face losing reimbursement, whereas she has spent "years analyzing each patient like a fine jewel." AR at 249. Physicians who "specialize in treating single case reports" are driven out of Medicare because of this illegal interference with the "doctor patient relationship," she elaborates. Id. This argument about the merit of single case reports is essentially a variation on the argument that the treating physician is the sole arbiter of what treatment is medically necessary regardless of whether the treatment has any scientific basis or any acceptance in the medical community. Rejecting that argument does not imply that physicians may not or should not treat patients as individuals.

One difficulty in evaluating individual case reports is that it may be impossible to know what the course of the illness would have been if treated by alternative means or if untreated. That problem is compounded when the biological treatment being evaluated has no standardized formulation and may be prepared using various protocols and blood derived from different numbers

and kinds of donors. Compare, for example, the description of TF preparation in J. Dwyer, Clinical and immunological response to antigen-specific transfer factor in drug-resistant infection with Mycobacterium xenopi, 47 The American Journal of Medicine 161-68 (1983) (A.P. Ex. 36) and H.F. Pabst, Successful treatment of Candidiasis with transfer factor, 2 British Medical Journal 442-43 (1973) (A.P. Ex. 89) with H.H. Kesarwala, Transfer factor therapy in hyperimmunoglobulinaemia E syndrome, 36 Clinical Experimental Immunology 465-72 (1979) (A.P. Ex. 63 - mistakenly listed as A.P. Ex. 61 in CRD record index). An additional uncertainty lies in evaluating the significance of improvements in individual patients when the course of their illnesses may vary for many other reasons, such as cyclical remissions, the onset of complications, or other changes in treatment or environment. For example, Dr. Calabrese points to a herpes case study as showing that the patient's "clinical course suggested that [TF] had been beneficial." AR at 208, citing L. Drew, "Herpes Zoster: Transfer factor therapy, 79 Annals of Internal Medicine 747-48 (1973) (A.P. Ex. 33). The study points out, however, that the course of herpes zoster infections, even in patients with immune deficiencies "is variable." A.P. Ex. 33. The researcher's conclusion is merely that the "evaluation of [TF] therapy for treatment of such patients needs further studies." Id.

Therefore, these studies, alone or with other evidence in the record, do not provide a sound basis for concluding that TF therapy is in fact effective for patients with abnormal cell-mediated immunity.

vi. Other arguments by the APs

Dr. Calabrese further opines that the ALJ incorrectly discounted "unpublished communication between transfer factor investigators" because "[i]mportant findings are not necessarily always published." AR at 214. She points to the fact that the authors of one article cite to personal communication from another researcher about results similar to those being reported by the authors. Id., citing Borkowsky, W. and Lawrence, H.S., Deletion of antigen-specific activity from leukocyte dialysates containing transfer factor by antigen-coated polystyrene, Journal of Immunology, Vol. 126, No. 2, 486, 489 (1981) in A.P. Ex. 20. A general weakness of unpublished research findings, however, is that they are untested by the scientific peer review process. Thus, the ALJ did not err in not treating unpublished research as a source of definitive scientific evidence.

The APs contend that TF therapy for their conditions cannot be considered experimental in light of the existence of NCD # 160.20, which bars coverage of TF therapy for use in multiple sclerosis cases as experimental and investigational. AR at 99. They reason that, since TF therapy for use in cell-mediated immunity was not barred by the NCD, it must be covered. Id. Dr. Calabrese agrees, as a matter of scientific opinion, that the research supports the exclusion from Medicare coverage of TF therapy for multiple sclerosis but asserts that "a multiple sclerosis patient who also has clinically significant abnormal cell mediated immunity" would still be covered for TF therapy under the NCD. AR at 201-02.

We find that the mere fact that CMS adopted no nationwide policy barring coverage of TF therapy for uses other than multiple sclerosis does not imply that its use in the clinical conditions presented by the APs (or for any other purpose) is necessarily covered or is not experimental. The Act and regulations contemplate that contractors may make coverage policies which are applicable only in their jurisdictions and which do not have the binding effect of NCDs in areas where CMS had not spoken through an NCD. Dr. Calabrese offers no support for her further assertion that some multiple sclerosis patients may still be reimbursed for TF therapy under Medicare.

3. Other contentions raised by the APs are either without merit or irrelevant to this proceeding.

A. We admit CMS Exhibit 1 to the record.

Dr. Calabrese objects to the ALJ's handling of CMS Exhibit 1. See, e.g., AR at 17, 23, 27-29, 32, 36, 49, 58. The exhibit is a copy of a June 2008 decision by an ALJ in OMHA, the office of the Department of Health and Human Services established to conduct hearings on individual Medicare claim determinations.[21] Pub. Law No. 108-173, § 931(a) and (b). The OMHA decision upheld a 2004 post-payment review determination by NHIC

[21] The OMHA decision is one step in the CMS review process of contractors' denials of individual claims explained earlier in this decision. For the claims at issue in the 2004 NHIC overpayment determination, the process consisted of review by a contractor hearing officer, review by an OMHA ALJ, review by the MAC, and review by a federal district court. Section 1869 of the Act (42 U.S.C. § 1395ff); 42 C.F.R. § 405.801-.872.

disallowing over $300,000 in reimbursement paid to Dr. Calabrese for TF therapy and related services that she provided to beneficiaries prior to 2004. ALJ Decision at 17. In January 2009, the MAC upheld the OMHA decision. Action and Order of Medicare Appeals Council in Dr. Calabrese, M.D., S.A., and 36 others (filed with CMS' Response to [APs'] Notice of Appeal) (MAC Decision).

Dr. Calabrese argued that the OMHA decision, which was (at that time) on appeal to the MAC, and also the subject of federal court challenges, should not be admitted by the ALJ as an exhibit in the LCD case. APs' Objection to . . . Exhibits Filed 11-07-08, at 7-11 (item 70 in CRD record index). She contends now as then that the OMHA decision is invalid because it was the product of gross fraud by NHIC and improperly signed by an OMHA ALJ other than the OMHA ALJ who conducted the hearing. See, e.g., AR at 22-23, 36, 49.

The ALJ read the OMHA decision as "turn[ing] on the lack of adequate documentation by Dr. Calabrese" to show that TF therapy had been medically necessary for those particular beneficiaries, rather than a determination about whether TF therapy itself could ever be medically necessary. ALJ Decision at 18. He excluded the OMHA decision on the ground that it was not relevant to the issue before him, i.e., the reasonableness of the contractors' determinations that TF therapy was never medically necessary for any beneficiaries. Id. at 9. However, the ALJ then proceeded to refer to the content of the OMHA decision because, as he stated, it is "an official record of the United States" (id. at 39) and "provide[s] some insight into the history of this case and it is cited hereafter in that context only" (id. at 9, see also id. at 17-18). While Dr. Calabrese asserts that ALJ's references to the OMHA decision are defamatory to her, she does not assert that the ALJ inaccurately depicted the content of that decision.

The ALJ did not admit the OMHA decision because he concluded it was not material to the issue of whether the LCD record was complete and adequate. We agree that it is not material to that issue. However, since the ALJ referenced the exhibit and its contents in his discussion (as do we), he should have admitted it into the record, and we do so now. Moreover, admitting the OMHA decision is consistent with ALJ's admission of certain of the APs' exhibits, such as pleadings from cases in federal court, which he also stated were irrelevant to the issue before him but which he admitted because they were of interest as background to the APs' position. See ALJ Decision at 7 n.5.

On appeal to the Board, Dr. Calabrese also argues for the first time that the ALJ's use of the OMHA decision was error because the decision had previously been filed by CMS in one of Dr. Calabrese's federal court actions and placed under seal by the court on June 19, 2008 pursuant to the parties' stipulation. See, e.g., AR at 36, 46, 93. Dr. Calabrese states that she so stipulated because the decision was "extremely defamatory and needed to be sealed." Motions for Sanctions filed in Docket No. A-09-123 on February 24, 2010, at 11.

We reject this basis for disturbing the ALJ Decision. First, we see no place in the record (and Dr. Calabrese cites none) where she objected before the ALJ that the OMHA decision was under court seal. Therefore, that argument has not been preserved for review. Second, Dr. Calabrese provides no authority for the proposition that an agency may not rely on one of its own records in an administrative proceeding simply because the document is also part of a sealed record in separate court proceedings. Third, the order sealing the decision is silent as to any effect on administrative proceedings, and we see nothing in this record that indicates that the federal court sealed the decision on the basis of any court determination that the content of the decision was flawed, defamatory or unreliable.[22]

B. The ALJ properly declined to review whether NHIC, prior to adopting the Second LCD, had a constructive LCD prohibiting reimbursement for TF therapy.

In addition to challenging the validity of the Second and Third LCDs, the APs asserted that NHIC had a sub rosa LCD on TF therapy (or, as the ALJ frames it, a constructive LCD) prior to NHIC's adoption, in October 2007, of the Second LCD. See, e.g., Request for LCD Appeal; Motion for Pre-Hearing Conference (items

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[22] Indeed, in a July 25, 2008 order, the court discussed many of the decision's overpayment findings that the ALJ subsequently discussed. Order Granting in Part and Denying in Part Parties' Cross-Motions for Summary Judgment, SACV 07-014444-CJC (ANx) (filed with CMS' Response). That document is available under the Public Access to Court Electronic Records at http://pacer.psc.uscourts.gov, which indicates that the court did not regard reference to these facts as suppressed by its seal. See Case 8.07-cv-01444-CJC-RNB Document 123.

2 and 16 in CRD Record). They represented that this constructive LCD was memorialized in NHIC article A38251/2 and used, in 2007, by a NHIC hearing officer in reviewing the NHIC 2004 overpayment determination in violation of DAB No. 2050.[23] See, e.g., Request for a Pre-Hearing Motion (item 15 in CRD record index). NHIC denied that A38251/2 was an LCD and denied that it had applied A38251/2 or any unwritten policy as an LCD. Memorandum Regarding Non-Existence of LCD (item 29 in CRD record index).

As to whether A38251/2 constituted an LCD as revised, the ALJ correctly ruled that he was bound by the Board's prior determination that revised A38251/2 was not an LCD because NHIC had withdrawn the language in the prior version of the article that barred coverage of TF therapy. ALJ Decision at 27, citing DAB No. 2050.

Noting that Dr. Calabrese admitted that no claims for TF therapy had been filed after October 30, 2003 (id. at 32), the ALJ also determined that "there [was] no evidence upon which a constructive LCD might be found" (id. at 27; see also id. at

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[23] The APs rely in part on assertions that, under section 1869(f) of the Act, "reimbursement is reinstated" after a contractor withdraws an LCD and that NHIC failed to reinstate reimbursement to them after withdrawing the First LCD. See, e.g., AR at 51. The phrase "reimbursement is reinstated" does not appear in section 1869(f) or the implementing regulations. As the Board explained in DAB No. 2050, upon withdrawal of an LCD "the aggrieved parties are entitled to have their prior claims reopened and readjudicated with no regard given to the withdrawn policy and . . . future claims by them or by other beneficiaries (after the effective date of the withdrawal) must be decided by NHIC without any reliance on the withdrawn policy." DAB No. 2050, at 18, citing 42 C.F.R. § 426(b)(1)(i) and (iv); see also ALJ Decision at 22, 28 citing 68 Fed. Reg. at 63,698, 63,712 (retiring or withdrawing an LCD results in the AP receiving individual claim review). However, section 1869(f) and the implementing regulations do not necessarily require the contractor to reimburse claims that were or would have been subject to the withdrawn LCD or preclude the contractor from conducting individual reviews of those claims to evaluate medical necessity for the particular beneficiary and compliance with other Medicare requirements.

33). In reaching this conclusion, he stated that to be such an LCD "a policy must also be applied or used by a contractor to automatically deny claims for benefits for treatment or services rather than conducting case-by-case medical review for whether treatment or service is reasonable and necessary." Id. at 20 (emphasis added).

This statement is incorrect. An LCD is any policy to deny coverage on a contractor-wide basis for a particular item or service. Section 1869(f)(2)(B) of the Act. The definition of an LCD does not require claims to have been submitted under it or to have been used to deny payment.[24] Moreover, the ALJ appears to use the term "automatically deny" to mean a prepayment denial, as if an LCD must be applied on a prepayment basis. See ALJ Decision at 22, 23, 27, 33. On the contrary, as CMS's manual makes clear, contractors may "apply LCDs to claims on either a prepayment or postpayment basis." MPIM § 13.10. This misunderstanding led the ALJ to conclude that the APs' allegation that a NHIC hearing officer applied article A38251/2 as an LCD in 2007 in reviewing NHIC's 2004 overpayment determination could not be a basis for finding a constructive LCD. ALJ Decision at 33 (stating that the claims denied by an NHIC hearing officer in the postpayment review "were actually paid and thus no LCD was applied to deny those claims.").

The ALJ's treatment of this allegation as irrelevant to the assertion that NHIC had applied a constructive LCD was harmless error, however, for a number of reasons.

First, even if ALJ Sickendick had found that NHIC did have a constructive LCD on TF therapy prior to the adoption of the Second LCD and that the NHIC hearing officer applied that constructive LCD, these claims would still be unpayable because, according to the OMHA decision that was upheld on appeal by the MAC, they were not documented in accordance with Medicare standards. CMS Ex. 1, at 8 n.4; MAC Decision. The MAC concluded that Dr. Calabrese failed to refute "the ALJ's basis

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[24] While an aggrieved party might attempt to prove the existence of a constructive LCD by showing that the contractor had used it to deny claims without conducting case-by-case reviews of individual beneficiaries' medical conditions, a party could also attempt to prove a constructive LCD by other means, for example, through statements by contractor personnel.

for denying coverage for the claims at issue, the appellant's failure to document the claims for coverage pursuant to section 1833(e)" of the Act. MAC Decision at 3.

Second, OMHA itself conducted a claim-by-claim review that provided a basis for the denial of these claims irrespective of the presence or absence of a constructive LCD. This fact is apparent from the detailed discussion in the OMHA decision as well as the attached 39-page chart setting forth beneficiary names, dates of service, and, for each service, the presence or absence of different types of documentation, such as "chart notes" and "testing sheet." CMS Ex. 1, at 34-72. The OMHA decision explicitly recognized that, even if "some sort of due process infringement may have occurred" at the hearing officer level, Dr. Calabrese's right to review of this overpayment determination was "not materially prejudiced" because OMHA conducted a de novo review of the denied claims that was not based on deference to any constructive LCD. CMS Ex. 1, at 8.

Third, the APs failed to support their factual allegation that, in reviewing NHIC's 2004 overpayment determination, the NHIC hearing officer applied revised A38251/2 retroactively as an LCD and failed to conduct a case-by-case review of the allegedly overpaid claims. While they quote selective passages from the hearing officer decision, they do not submit the decision. Therefore, we cannot evaluate directly the scope of the hearing officer's review of these claims. Moreover, the OMHA decision indicates that the hearing officer did consider the individual claims, including documentation of medical condition, needs, and treatment of individual beneficiaries, rather than merely applying an alleged NHIC policy requiring claims for TF therapy to be denied as medically unnecessary in every case. The OMHA decision stated:

> . . . *each [Date of Service] in her post-payment review must meet the coverage criteria in order for the payment to be found proper.* So even if transfer factor is a standard medical treatment as contended by appellant and her medical expert, that determination by itself is not sufficient to support Medicare coverage since the contractor nevertheless has a duty to determine if payments were properly made to appellant. And, it is a fact that the contractor can only make this determination by reviewing appellant's claims against the medical records provided. If her records did not demonstrate medical need for the services at issue, *which is what was found at the lower Medicare appeal levels*, the services reviewed were not eligible for

> payment, i.e., not covered services; and, therefore, as the contractor determined reimbursements to appellant were made in error. The overpayment assessed against her represents the reimbursements made in error. Furthermore, contrary to appellant's assertions, there is nothing in the record suggesting that the claims in the review period were denied for any reason other than the contractor's determination that the supporting documentation is deficient, i.e., that it failed to show that the required coverage and payment criteria had been met at the time the services were rendered.

CMS Ex. 1, at 8 n.4 (emphasis in original).

As to other potential claims for services rendered between the time Dr. Calabrese was put on prepayment review and the Second LCD, the record is unclear as to whether Dr. Calabrese refrained from providing TF therapy to Medicare beneficiaries or provided services but refrained from submitting claims to NHIC.[25] In either case, we see no reason for further review of NHIC's alleged use or non-use of A38251/2 prior to the issuance of the Second LCD.

C. The ALJ correctly ruled that the APs had no standing to challenge the LCD on the basis of alleged misconduct committed by NHIC during the process of adopting the Second LCD.

The APs argue on appeal the ALJ erred by concluding that they had no standing to challenge the process NHIC used in developing the LCD. Dr. Calabrese alleges on behalf of the APs that NHIC's (and Palmetto's and CMS's) actions in developing the LCD violated the United States Constitution, "BIPA 2000 section 522," other federal civil and criminal statutes, and the MPIM

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[25] See A.P. Ex. 194, at 5 (one AP states that, after the First LCD, "I told Dr. Calabrese, as did other Medicare beneficiaries, that I would pay her for [TF] therapy. She explained she could not accept money from any Medicare patients without dropping out of the Medicare program."); AR at 53 (stating that Dr. Calabrese "has been illegally obstructed from submitting any bills from 2003 to the present on behalf of her patients . . . .").

(which sets out the process for developing an LCD).[26] See, e.g., AR at 25, 30, 41, 71, 79, 84-85, 91. For example, she alleges that the ALJ erred by not considering her allegations that the NHIC Medical Director improperly "excluded all our experts, [herself], and [the APs] from participating in the (MPIM) public comment process" for the Second LCD (AR at 40-41, see also id. at 71, 91) and that he engaged in "intentional and negligent criminal and civil violations against our class of Medicare patient" in developing the LCD (AR at 79).

Relying on the following authorities, the ALJ correctly reasoned that Congress did not give aggrieved parties standing to challenge the process that a contractor used to develop an LCD or give the ALJ authority to review that process. ALJ Decision at 27-28. Section 1869(f) of the Act, which establishes an aggrieved party's right to ALJ review of an LCD, provides only for review of the reasonableness of the LCD. Moreover, section 1869(f) does not set forth standards for developing an LCD, provide for review of the process used by a contractor in developing an LCD, or even require CMS to adopt regulations setting forth procedures for developing an LCD. Similarly, CMS's LCD regulations do not include such procedures or grant an aggrieved party the right to challenge an LCD on the basis that it was not properly developed. 42 C.F.R. § 426.325. CMS did adopt a policy for LCD development in section 13.7 of the MPIM. As to this policy, the ALJ noted that the procedure "is detailed but establishes no right for an aggrieved party to challenge a LCD based upon the procedure by which it was developed and it recognizes no such right." ALJ Decision at 28. He correctly concluded, "Accordingly, . . . an aggrieved party has no right to challenge a LCD on the basis that it was not properly developed and . . . I have no jurisdiction to review a LCD on that basis." Id., citing LCD Appeal of Non-coverage of Intravenous Immunoglobulin (LCD Database Id. No. L924), DAB No. 2059 (2007).[27]

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[26] Because we agree with the ALJ that aggrieved parties do not have standing to challenge the process by which an LCD was developed, we do not discuss their specific allegations about NHIC's alleged misconduct. We do not reach any opinion on whether the merits of these allegations might be reached in other proceedings in other fora.

[27] We do not conclude that no circumstances could exist under which CMS's directions to contractors in the MPIM might be

(Continued . . .)

Importantly (and contrary to the impression given by the APs' arguments), the section 1869(f) review process does allow aggrieved parties to challenge material contractor errors and misconduct, i.e., alleged actions or omissions that might cause the LCD record before the ALJ to be unreliable. As the ALJ noted, in an LCD proceeding, an ALJ reviews the reasonableness of the LCD on the basis of scientific evidence submitted by both parties. ALJ Decision at 50. If a contractor has unintentionally or even intentionally omitted allegedly relevant scientific evidence in its LCD development process or in its submission to the ALJ, the aggrieved party's recourse is to submit that evidence to the ALJ. The ALJ must then review all the evidence and the aggrieved parties' arguments as to the authenticity of the contractor's evidence and the weight to accord it. As the ALJ stated, "I do consider whether [CMS's] documents are authentic. I also consider whether each [CMS] document . . . is credible and whether the document is entitled to weight in applying the reasonableness standard . . . ." ALJ Decision at 8 n.7.

Significantly, in this case the APs submitted extensive scientific evidence to the ALJ and objected to the admission of several CMS exhibits. The ALJ excluded a number of CMS's exhibits (or said he would give them diminished or no weight) on the basis of these objections and evaluated the remaining evidence submitted by both parties, explaining at length how he evaluated the persuasiveness of the evidence. ALJ Decision at 9-10; 41-57. As explained above, we have carefully reviewed the same record and found no material error in the ALJ's conclusions based on it.

Thus, in this section 1869(f) process, the APs have had the opportunity to dispute NHIC's submissions and omissions to the extent that they might have affected the authenticity and the reliability of the evidence before the ALJ.[28]

(Continued . . .)

relevant in evaluating whether a record is complete and adequate to support an LCD under the reasonableness standard, but we find no statutory or regulatory basis for an aggrieved party to challenge the LCD development process per se.

[28] Dr. Calabrese specifically argues that NHIC should have given her personal notice when proposing the Second LCD. AR at

(Continued . . .)

D. The ALJ did not err by refusing to impose sanctions on the CMS Attorney.

Before the ALJ and on appeal, Dr. Calabrese, acting on behalf of the APs, has repeatedly sought to have the CMS attorney in this case replaced, investigated, and/or sanctioned. See, e.g., AR at 17, 31, 27-29, 58, 93-94. The ALJ refused to do this, as do we.

Before the ALJ, Dr. Calabrese alleged that the CMS attorney "introduced fraudulent documents into this case and misled [the ALJ] with respect to OMHA decision 06-03-08 [CMS Ex. 1] . . . ." ALJ Decision at 38, citing "Motion for Hearing that CMS Region IX Attorney Angela Belgrove a) Be Replaced or b) Be Sanctioned." Dr. Calabrese continues to argue that the OMHA decision is the product of fraud and, therefore, the CMS attorney's use of it here and before the federal court should result in sanctions. See, e.g., AR at 46-49, 93-94. The ALJ correctly rejected this argument, writing:

> Dr. Calabrese's allegations that Attorney Belgrove introduced a fraudulent document or misled me [are] frivolous. I am well aware of Dr. Calabrese's arguments regarding the legitimacy of the OMHA decision . . . . I am aware that Dr. Calabrese disagrees with the decision. Nevertheless, the decision is an official record of the United States and it will remain so, even if Dr. Calabrese

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(Continued . . .)

41; see MPIM at §§ 13.7.4 - 13.8.1.4 (setting forth CMS's LCD adoption policy). The fact that it did not (which NHIC does not deny) allegedly resulted in her not commenting or submitting information to NHIC's Carrier Advisory Committee (CAC) about the LCD and the exclusion of her evidence. Id. However, under the section 1896(f) process, she was free to present this information to the ALJ and to dispute NHIC's assertions about the lack of public opposition to and the CAC's endorsement of the Second LCD. See CMS Ex. 18. Moreover, Dr. Calabrese identifies no authority for her assertion that NHIC violated any law or regulation by not giving her such personal notice and does not allege that NHIC failed to give the notice required by the MPIM to relevant groups or on its website. See MPIM at § 13.7.4.1.C.

> is successful at some time in the future overturning the decision. The document clearly reflects some of the history leading to the adoption of the LCD at issue in this case. . . . Based upon my review of CMS Ex. 1, Attorney Belgrove made no misrepresentation about what the document is or says . . .

ALJ Decision at 39.

On appeal, Dr. Calabrese argues that the CMS attorney's use of the OMHA decision was also improper because it had been sealed by a federal court. We have already discussed why this seal was not a barrier to the ALJ's use of the OMHA decision. Dr. Calabrese may, of course, ask the federal court to consider whether this use by a party before it violated its order.

The ALJ also rejected Dr. Calabrese's allegation that the CMS attorney had improperly removed and refused to replace what Dr. Calabrese characterizes on appeal as an "exculpatory document." AR at 93, citing ALJ Decision at 38. The document at issue is an April 2008 email by an NHIC employee with the surname of DeBell.[29] CMS included the email in a set of documents that it filed in response to the ALJ's October 21, 2008 order to file the supplemental record for the Third LCD. ALJ Decision at 39. Because documents filed by NHIC previously and by CMS in October 2008 were not properly marked as evidence and many appeared to be "not relevant to or weighty on the issue before me," the ALJ subsequently ordered CMS to "mark as evidence the documents from the LCD record and supplemental record that it considered relevant to the issue before me at this phase of the proceedings, and resubmit the documents." Id. at 39 n.24. CMS did not resubmit all of the documents that had been previously submitted, including the April email, nor did it rely on this email in any way. Id. at 39. The fact that the CMS attorney had previously served this email on Dr. Calabrese belies any notion that the attorney was trying to mishandle "exculpatory" evidence; Dr. Calabrese was free to submit the email for the record if she wanted to rely on it.

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[29] On appeal, the APs argue that statements in the email show that NHIC was violating "BIPA 2000 Sec. 522" (i.e., section 1869(f)). See, e.g., AR at 93. They cite to no specific language in section 1869(f) supporting this argument.

We thus decline to impose any sanction ourselves and find no error in the ALJ's similar refusal to sanction the CMS attorney.

E. The ALJ correctly rejected arguments that he should invalidate the LCD and grant other relief based on alleged violations of the United States Constitution.

Before the ALJ, the APs alleged repeatedly that their rights to equal protection and due process under the United States Constitution had been violated. See, e.g., Declaration of Dorothy Calabrese, M.D., on Appellants' 'Class of One' due process and equal protection under the 5th Amendment to the US Constitution dated October 10, 2008 (item 61 in CRD record index). On appeal, they repeatedly assert that the ALJ erred by refusing to grant the relief requested pursuant to these arguments. See, e.g., AR at 6, 10-14, 27-29, 40-42, 74, 81. We disagree.

The ALJ correctly concluded that "to the extent that Dr. Calabrese intends to challenge either the Act or the Secretary's regulations, I have no jurisdiction to address her challenge." ALJ Decision at 40, citing 42 C.F.R. § 426.405(d)(13) (stating "the ALJ does not have the authority to [f]ind invalid applicable Federal statutes [and] regulations . . . ."); see also Sentinel Medical Laboratories, Inc., DAB No. 1762, at 9 (2001) (finding it "well established that administrative forums, such as this Board and the Department's ALJs, do not have the authority to ignore unambiguous statutes or regulations on the basis that they are unconstitutional"), aff'd, Teitelbaum v. Health Care Financing Admin., supra.

On the other hand, an ALJ and the Board may consider constitutional claims challenging the manner in which a statute or regulation is interpreted or applied in a particular case. See Sentinel, DAB No. 1762, at 11-12. To the extent the APs are challenging the application of section 1869(f) or the implementing regulations in the adoption of the Second and Third LCD, we see no merit to the arguments or any material error in the ALJ's treatment of the arguments for the reasons discussed below.[30]

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[30] The APs allege many due process violations and "difference[s] in treatment" between "appellants' class of Medicare patient" and "all other classes of Medicare patients." See, e.g., AR at 10 (first page of a four-page chart of alleged

(Continued . . .)

As to Dr. Calabrese's due process claims, the ALJ stated that "to the extent that Dr. Calabrese challenges the process accorded her by this proceeding, I have accorded the APs the process due them under the Act and regulations." ALJ Decision at 40. We agree. The ALJ provided an opportunity to present evidence in support of TF therapy and to challenge CMS's evidence as inauthentic or unpersuasive, i.e., the process due under 42 C.F.R. Part 426, subpart D. The ALJ had no authority under the regulations to conduct further evidentiary proceedings once he concluded that the APs had failed to show that the record before the ALJ was not complete and adequate to support the validity of the LCD. 42 C.F.R. § 426.425.

Moreover, even were the equal protection arguments relevant here, we see no merit to them. As the APs state, equal protection concerns arise when the government treats similarly situated people differently without a rational basis. AR 6-7. They then assert that NHIC, Palmetto, and CMS, without a rational basis, have treated Medicare beneficiaries who seek reimbursement for TF therapy differently by treating TF therapy as not medically necessary. See, e.g., AR at 6-7, 10-14. No beneficiaries are entitled to reimbursement for treatments that are not medically necessary. The purpose of this proceeding has been to review whether the contractors' determination that TF therapy is not medically necessary is valid and, as such, a rational basis exists for treating claims for TF therapy differently from other claims for goods and services that are considered medically necessary.

(Continued . . .)

differences). The allegations involve a wide array of alleged wrongdoers, circumstances, and periods of time. For example, they include allegations about corruption in the CMS NCD process and false testimony before the contractor hearing officer and OMHA ALJ. Id. at 10-11. As with the specific allegations about NHIC's development of the LCD, we find these claims without relevance to the issues before us, and we do not address the merits.

F. The ALJ correctly rejected demands for review of irrelevant issues and for relief he had no authority to grant.

The appeal request contains repeated statements such as that "[t]his case and all our collateral Medicare cases represent the worst case of CMS and CMS carrier corruption against innocent senior and disabled patients in the history of Medicare Part B" and that this corruption has resulted in "the preventable premature morbidity and mortality" of the patients Dr. Calabrese represents. See, e.g., AR at 2, 437; Supplemental Declaration of Dorothy Calabrese, M.D. dated February 24, 2010, at 3. Before the ALJ and the Board, Dr. Calabrese made numerous assertions of personal knowledge in support of these allegations of civil/criminal wrongdoing and corruption by NHIC personnel, CMS personnel, attorneys for CMS and for the United States Department of Justice, an ALJ at OMHA, and private allergists, as well as corruption in the process for the development of LCDs and NCDs (claiming, for example, that she has been told that practitioners must "buy" codes and coverage determinations). See, e.g., ALJ Decision at 26, 30; AR at 10, 65-66.[31] Additionally, she has demanded relief that exceeds the relief provided by law for aggrieved parties in an LCD review and that the Board has no authority to grant, such as "an independent investigation interagency - or through the Department of Justice, as to our charges of CMS and CMS carrier criminal and civil violations since 2003 at the agency level." AR at 434.

We do not question the sincerity of Dr. Calabrese's belief that TF therapy is medically necessary for the patients she represents, the depth of her commitment to securing Medicare reimbursement for such therapy, or her claims that she has made personal and professional sacrifices in challenging TF therapy LCDs. Plainly, she has come to the conclusion that the denial of coverage for TF therapy can only reflect wrongdoing at all

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[31] The record does not contain any evidence beyond Dr. Calabrese's uncorroborated assertions for her allegations that contractor staff or others outside NHIC told her that coverage determinations were for sale or that particular providers received favorable treatment in "quid pro quo LCDs to certain classes of Medicare patients . . . ," much less any evidence that, if any such statements were made, they had a basis in fact. AR at 10.

levels. She has not, however, presented evidence beyond her own allegations to support claims that the record has been tainted by fraud or corruption.[32] Accordingly, we reject her claims of wrongdoing.

As we (and the ALJ) have tried to explain, the LCD review authority granted to the ALJs and the Board under section 1869(f) of the Act is narrow, and the standards aggrieved parties must meet to prevail are demanding. The ALJ is limited to determining whether the record before him is complete and adequate to support the LCD under the reasonableness standard. Under this standard, an ALJ must uphold the LCD if "the findings of fact, interpretations of law, and applications of fact to law by the contractor or CMS are reasonable based on the LCD or NCD record and the relevant record developed before the ALJ or the Board." 42 C.F.R. § 426.110. In evaluating whether such findings, interpretations, and applications are reasonable, the ALJ must defer to the determinations by the contractor and CMS "[s]o long as the outcome is one that could be reached by a rational person . . . ." 68 Fed. Reg. at 63,703. As explained in our discussion of the scientific evidence, the APs failed to show that a rational person could not have reached the outcome reflected in the Third LCD - that TF therapy has not been shown to be medically necessary in accordance with section 1862(a)(1)(A) - and, therefore, the contractor has not acted unreasonably in adopting the LCD.

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[32] The APs argue that the ALJ wrongly denied discovery to inquire into possible fraud or impropriety at the contractor level and similar objections, and seek remand for discovery and a hearing. AR at 21, 101-03; ALJ Decision at 6, 8, 10, 26, 38. The ALJ explained correctly that discovery is not contemplated until the second stage of the LCD review process. ALJ Decision at 8 n.7. He did consider the APs' allegations in assessing whether to treat documents submitted by the government as authentic and credible. Id. Since the ALJ's analysis, and our review of it, focused largely on the scientific literature, we agree with the ALJ that any alleged irregularities in the contractor's process for developing the LCD record that might emerge from discovery would not undercut the basis for the conclusion that the record is complete and adequate to support the validity of the LCD even after consideration of the evidence proffered by the APs in an effort to show the contrary.

Conclusion

For the reasons set forth above, we uphold the ALJ Decision.

/s/
Judith A. Ballard

/s/
Sheila Ann Hegy

/s/
Leslie A. Sussan
Presiding Board Member