

MSCI Biotech Advance Indexes

June 2023



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1 Introduction

The MSCI Biotech Advance Indexes (the 'Indexes'¹) aim to represent the performance of a set of companies that are associated with research, development, and commercialization of products for treating a broad range of diseases and disorders-related to:

- Cancer
- Infections including HIV and related conditions
- Blood
- Neurology
- Musculoskeletal system
- Sensory Organs
- Immune system
- General diseases including cardiovascular, diabetes, skin and respiratory diseases

¹The Indexes are governed by a set of methodology and policy documents ("Methodology Set"), including the present index methodology document. The methodology set for the Indexes can be accessed from MSCI's webpage <https://www.msci.com/index-methodology> in the section 'Search Methodology by Index Name or Index Code'.



2 Constructing the Indexes

Each Index is constructed by selecting securities from an underlying MSCI equity index ('Parent Index'²).

MSCI may seek input from outside market experts on the ongoing evolution of the theme underlying the Index. However, such input is advisory only in nature. MSCI alone decides whether to use such input at all or to what extent. Receipt of such input, like any other feedback on MSCI indexes, may or may not lead to a change to the Index or Index methodology.

2.1 Company Level Data

The following company level data³ is used to determine the scores that are subsequently used in Index construction.

- Clinical Trials Information – Clinical Trials where a company is either a lead sponsor, or alternatively, a collaborator with another commercial entity.
- Product Revenue Information
 - Historical product-level revenue, worldwide on an annual basis
 - Forecasted product-level revenue from currently marketed products as well as from products which are still under development, worldwide on an annual basis
- Mapping of Clinical Trials to Products
- Mapping of Products to Indications

2.2 Eligible Universe

The Eligible Universe is determined by selecting all securities from the Parent Index which belong to GICS® Sector⁴ 'Health Care'. Securities in the Eligible Universe are assigned their respective weight from the Parent Index. Security weights are further renormalized to sum to 100%.

2.2.1 Defining a Category

A Category is defined as a set of specific Indications as defined in Appendix III. Please see Appendix I for details of Indications, Products and Clinical Trials provided by Evaluate.

² Use of some indexes as Parent Indexes may result in a low number of constituents, which may affect replicability.

³ See Appendix I for definitions and more detail about clinical trials, product category and clinical trials mapping and indications. Clinical trials listed on following global registries are in scope : <https://clinicaltrials.gov/>, EUDRA - <https://www.clinicaltrialsregister.eu/ctr-search/search> and JAPIC - <https://www.clinicaltrials.jp/cti-user/common/Top.jsp>

⁴ GICS, the global industry classification standard, jointly developed by MSCI Inc. and S&P Global.



2.2.2 Calculation of Security-level Scores

The following scores are calculated at the security-level for each Category:

- Category Score - calculation steps described in Appendix II.
- Category Share Score - calculation steps described in Appendix II.
- Rank:
 - If Category Score < 50%, Rank =0,
 - If $50\% \leq$ Category Score <75%, Rank =1,
 - If Category Score \geq 75%, Rank =2

2.3 Security Selection

2.3.1 Selected Universe 1

The following steps are used within each Category to construct the Selected Universe 1:

1. All securities in the Eligible Universe with a Rank of 0 are excluded.
2. The remaining securities are sorted in descending order of their:
 1. Rank, and then by
 2. Weight in the Eligible Universe
3. Securities in the top half of this ranked set are included in the Selected Universe 1. If the ranked set consists of an odd number of securities, the number of securities selected in the top half will be rounded down to the nearest integer.

An Aggregate Score is calculated for each security in Selected Universe 1, as: maximum of Category Scores across all Categories that lead to the selection of the security in Selected Universe 1.

2.3.2 Selected Universe 2

The following steps are used to construct the Selected Universe 2:

1. Securities from the Eligible Universe which are included in Selected Universe 1 are excluded.
2. From the remaining securities, those which satisfy both conditions below are included in Selected Universe 2:
 1. maximum of a security's Category Share Score, across all Categories is \geq 20%, and
 2. the security has at least 2 Categories for which its Category Share Score is \geq 10%

Securities from the Selected Universe 1 and the Selected Universe 2 are combined to form the Selected Universe of the Index.



2.3.3 Weighting Scheme

Securities are weighted in the following steps:

- Securities from Selected Universe 2 are assigned their weight in the Eligible Universe.
- Securities in Selected Universe 1 are weighted in proportion of the product of their Aggregate Score and their weight in the Eligible Universe. The weight of securities in Selected Universe 1 are then multiplied by a factor of $(1 - \text{aggregate weight of Selected Universe 2})$.

2.3.4 Capping of Securities

Additionally, securities' weights are capped at the security level to mitigate concentration risk in the Index. The security weight in the Index is capped at 10% at each rebalance only; capping is not applied between rebalances. Please refer to MSCI Capping Indexes methodology (<https://www.msci.com/index/methodology/latest/Capped>) for further details.



3 Maintaining the Index

3.1 Semi-Annual Index Review

The Index is reviewed on a Semi-Annual basis in May and November and the changes are implemented at the end of May and November. In general, the pro forma Index is announced nine business days before the effective date.

During the Semi-Annual Index Review, the Eligible Universe and the Selected Universe are updated.

In general, MSCI uses the latest available company data as of the previous end of the month date before rebalancing date of the Semi-Annual Index Review. In case of unavailability of previous month-end data on a particular rebalance date, the latest available data is used.

3.2 Ongoing event-related maintenance

The general treatment of corporate events in the Index aims to minimize turnover outside of Index Reviews. The methodology aims to appropriately represent an investor's participation in an event based on relevant deal terms and pre-event weighting of the Index constituents that are involved. Further, changes in Index market capitalization that occur as a result of corporate event implementation will be offset by a corresponding change in the Variable Weighting Factor (VWF) of the constituent.

The following section briefly describes the treatment of common corporate events within the Index.

No new securities will be added (except noted below) to the Index between Index Reviews. Parent Index deletions will be reflected simultaneously.

**EVENT TYPE****EVENT DETAILS****New additions to the Parent Index**

A new security added to the Parent Index (such as IPO and other early inclusions) will not be added to the Index.

Spin-Offs

All securities created as a result of the spin-off of an existing Index constituent will be added to the Index at the time of event implementation. Reevaluation for continued inclusion in the Index will occur at the subsequent Index Review.

Merger/Acquisition

For Mergers and Acquisitions, the acquirer's post event weight will account for the proportionate amount of shares involved in deal consideration, while cash proceeds will be invested across the Index.

If an existing Index constituent is acquired by a non-Index constituent, the existing constituent will be deleted from the Index and the acquiring non-constituent will not be added to the Index.

Changes in Security Characteristics

A security will continue to be an Index constituent if there are changes in characteristics (country, sector, size segment, etc.) Reevaluation for continued inclusion in the Index will occur at the subsequent Index Review.

Further detail and illustration regarding specific treatment of corporate events relevant to this Index can be found in the MSCI Corporate Events Methodology.

The MSCI Corporate Events methodology book is available at:
<https://www.msci.com/index-methodology>.



Appendix I Data sources and Data Definitions

Data sources used in Index construction

The Index uses company-level pharmaceutical product and clinical trials data provided by Evaluate⁵ via the data services: Omnium Risk, Evaluate Omnium and Omnium Return.

Evaluate is a leading provider of commercial intelligence and analytics about the global pharmaceutical industry through its Evaluate Pharma (EP) and Evaluate Omnium services. Evaluate Pharma offers a perspective on the pharmaceutical market's historic and potential future development by providing five-year consensus forecasts, company financials, pipeline estimates and deals data. Evaluate Omnium provides a gauge of the development risk and potential commercial opportunity across the phases of the clinical lifecycle.

Definition of company level product and trials data items

Product Classification by level 1 Indication

Evaluate Pharma provides a mapping between the therapeutic activity of a product and a primary indication. Level one Indication can be defined as the top of a three level classification that represents the disorders for which the product is used or developed. Each level one indication is divided into multiple level 2 indications which in turn are divided into multiple level 3 indications.

Product/Clinical Trials mapping

EP maps a product to a clinical trial using analysis of each product mentioned in the clinical trial description, triangulated with company and indication information.

Product Revenue Information

EP provides company/product level historical reported, and consensus forecast sales at the product, or product group level. Forecasts may be up to 6 years forward.

⁵ <https://www.evaluate.com/>



Appendix II Calculating Company Level Scores

For a given Category, company-level scores are calculated in following steps:

1. Selected Indication is an indication mapped to the Category as described in Appendix III.
2. Indication Trial Score = Number of Selected Clinical Trials/Number of In-Scope Clinical Trials, where:
 - a. Number of In-Scope Clinical Trials = Number of clinical trials where the company is either a lead sponsor, or alternatively, a collaborator with another commercial entity and which meet the following conditions are considered In-Scope Clinical Trials:
 - I. Start Date: Trials which have been started in the 36 months preceding the rebalance date
 - II. Study Type: Interventional
 - III. Lead Sponsor: Industry
 - IV. Status of Study: Trial status should not be Terminated, Suspended or Withdrawn
 - V. Type of Trial: Commercial Trials⁶
 - b. Number of Selected Clinical Trials⁷ = Number of In-Scope Clinical Trials which are mapped to the Selected Indication.
3. Selected Products are all products which are mapped to the Selected Indication
4. Indication Share of Enrollments = Total number of participants enrolled in Selected Clinical Trials/Total number of participants enrolled in Selected Clinical Trials mapped to all securities in a global MSCI universe of 40,000+ issuers.
5. Indication Financial Relevance Score = Product-level Revenue from Selected Products/Product-level Revenue from All Products, where:
 - a. Product-level Revenue from All Products = The sum of Product-level Cumulative Revenue of all products mapped to that company
 - b. Product-level Revenue from Selected Products = The sum of Product-level Cumulative Revenue from all Selected Products mapped to that company
 - c. Product-level Cumulative Revenue⁸ is obtained by aggregating:
 - I. The sum of Historical product-level revenue for Rebalance Year and one year prior to Rebalance Year,and

⁶ Trials are flagged as Commercial or Non-commercial by EP. According to EP, in order for a trial to be classified as 'Commercial' one of the interventions under investigation in the trial must relate to a product in EP's product portfolio of one of the Sponsors or Collaborators listed on the trial protocol on ClinicalTrials.gov.

⁷ For securities having no in-scope clinical trials, the number of selected clinical trials used for scoring is taken as zero.

⁸ For securities having no projected or reported revenue for the period in scope, product-level cumulative revenue is taken to be zero



- II. The sum of forecasted product-level revenue from one year after Rebalance Year to six years after Rebalance Year

Rebalance Year is defined as the year of the rebalance date.

6. Indication Share of Revenue = Product-level Revenue from Selected Products / Sum of Product-level Revenue from Selected Products mapped to all securities in a global MSCI universe of 40,000+ issuers.
7. Indication Score = Max (Indication Trials Score, Indication Financial Relevance Score)
8. Indication Share Score = Max (Indication Share of Enrollments, Indication Share of Revenue)
9. Category Score = Max of all Indication Scores of Indications mapped to that Category, as shown in Appendix III
10. Category Share Score = Max of all Indication Share Scores of Indications mapped to that Category, as shown in Appendix III



Appendix III Category and Indication

	Indication	Category
1	Cancer	Cancer and Immunology
2	Immunology	
3	HIV & related conditions	HIV & related conditions and Infections
4	Infections	
5	Blood	Blood
6	Sensory organs	Sensory organs
7	Miscellaneous	Miscellaneous
8	Musculoskeletal	Musculoskeletal
9	Neurology	Neurology
10	Cardiovascular	General Medicine ('Gen Med')
11	Diabetes	
12	Respiratory	
13	Skin	
14	Hormone	
15	Psychiatry	
16	Urinary tract	
17	Hepatic & Biliary	
18	Gastro-intestinal	
19	Reproduction	
20	Surgery	Not in scope of this methodology

These Indications cover all Level I indications provided by Evaluate Pharma.



Appendix IV Construction of the China All Shares IMI Biotech Advance Index

This Index is constructed using the steps in section 2 but with the following differences compared to sections 2.3.1, 2.3.2 and 2.3.3:

4.1 Selected Universe

Securities from the Eligible Universe with a Category Score of 50% or more, for any Category are included in the Selected Universe.

4.2 Weighting Scheme

Securities in the Index are weighted by the product of their Aggregate Score and their weight in the Eligible Universe where:

Aggregate Score is calculated as:

maximum of Category Scores across all Categories that lead to the selection of the security in the Selected Universe.



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