# CANADIAN IMPORTED SURGICAL ALLOGRAFT AND ACELLULAR DERMAL MATRIX STUDY 2013

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Published April 2013 by

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Production of this advice/report has been made possible in part through a financial contribution from Health Canada.

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## MARKET DEFINITIONS

The Canadian surgical imported allograft market comprises nonproprietary allografts (including bone and soft tissue grafts), proprietary allografts (including demineralized bone matrices [DBMs] and cancellous/corticocancellous chips, powders, etc.), machined bone grafts, bone morphogenetic proteins (BMPs), other allografts (i.e., allograft dura), while the acellular dermal matrix (ADM) market comprises allograft-based ADMs and reinforcement grafts.

For a more in-depth discussion on these materials and the procedures they are used in, please refer to the introduction chapter. This chapter focuses primarily on imported products that are used across the country and does not include materials utilized in cardiovascular or ocular procedures.

## IMPORTED SURGICAL MUSCULOSKELETAL AND SOFT TISSUE ALLOGRAFT AND ADM MARKET

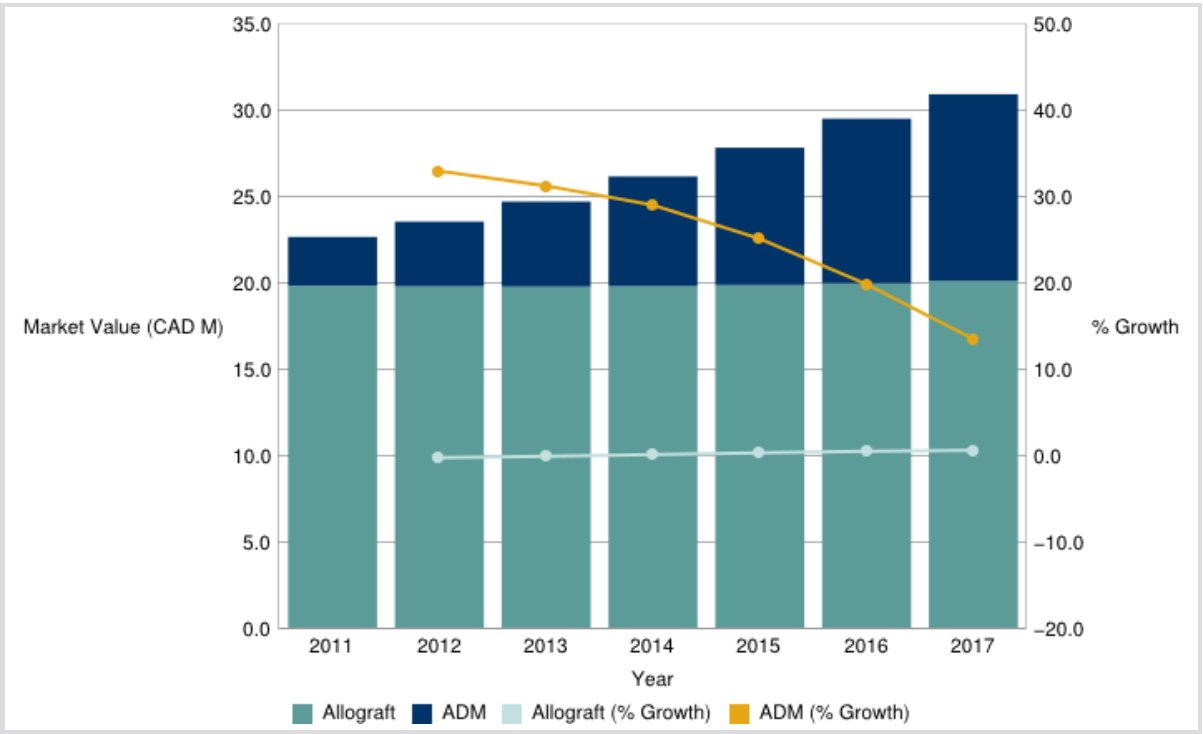
The Canadian surgical imported musculoskeletal, soft tissue allograft, and acellular dermal matrix (ADM) market comprises nonproprietary allografts, proprietary allografts, machined bone allografts, bone morphogenetic proteins (BMPs), other allografts (i.e., allograft dura), and allograft-based ADMs (which includes those used in breast reconstruction and reinforcement grafts). These products can be used in general orthopedics, craniomaxillofacial (CMF) surgery, sports medicine, neurosurgery, and, in the case of ADMs, plastic surgery, general orthopedics, CMF, and sports medicine.

The value of the import market will experience moderate growth through 2017 due to a rise in the number of procedures, such as spinal fusions and large-joint reconstructions, performed—stemming mostly from a growing aging demographic—that often require the use of allografts and ADMs. Additionally, the growing shift away from the use of autograft, which is losing favor due to the need for a second donor morbidity site, will also encourage the use of the aforementioned materials. Furthermore, allograft products are being increasingly incorporated into procedures to supplement autografts because there is sometimes an insufficient volume of autograft bone available for the procedure.

Nevertheless, growth of the imported allograft market will be limited due to the rising popularity of allograft substitute products, especially synthetics. The main benefit of synthetic products is the fact that they mitigate the risk of disease transmission. Additionally, with diminishing hospital budgets, physicians are looking for cost-effective allograft products from sources such as the domestic tissue banks. To address the issue of decreasing budgets among health care facilities, manufacturers and distributors in the imported allograft space will continue to reduce prices through initiatives such as tenders and volume discounting, which will result in restricted annual revenue growth. Furthermore, Canadian tissue banks are also increasingly working with surgeons and hospitals to ensure that needs are being met, either through better coordination and organization of the collection of donor tissue,

potentially diminishing the need for imported allograft tissue. Despite some of the challenges affecting revenue expansion, the Canadian musculoskeletal and soft tissue imported allograft segment will grow marginally while the ADM market will experience high double-digit expansion, resulting in an aggregate value of over $30 million by the end of the forecast period.

**Figure 1: Imported Surgical Musculoskeletal and Soft Tissue Allograft and ADM Market, by Product Type, Canada (CAD), 2011–2017**




Notes: ADMs include reinforcement grafts used in general orthopedic, sports medicine, and CMF procedures, as well as allograft-based ADMs used in breast reconstruction procedures (plastic surgery).

Source: Millennium Research Group

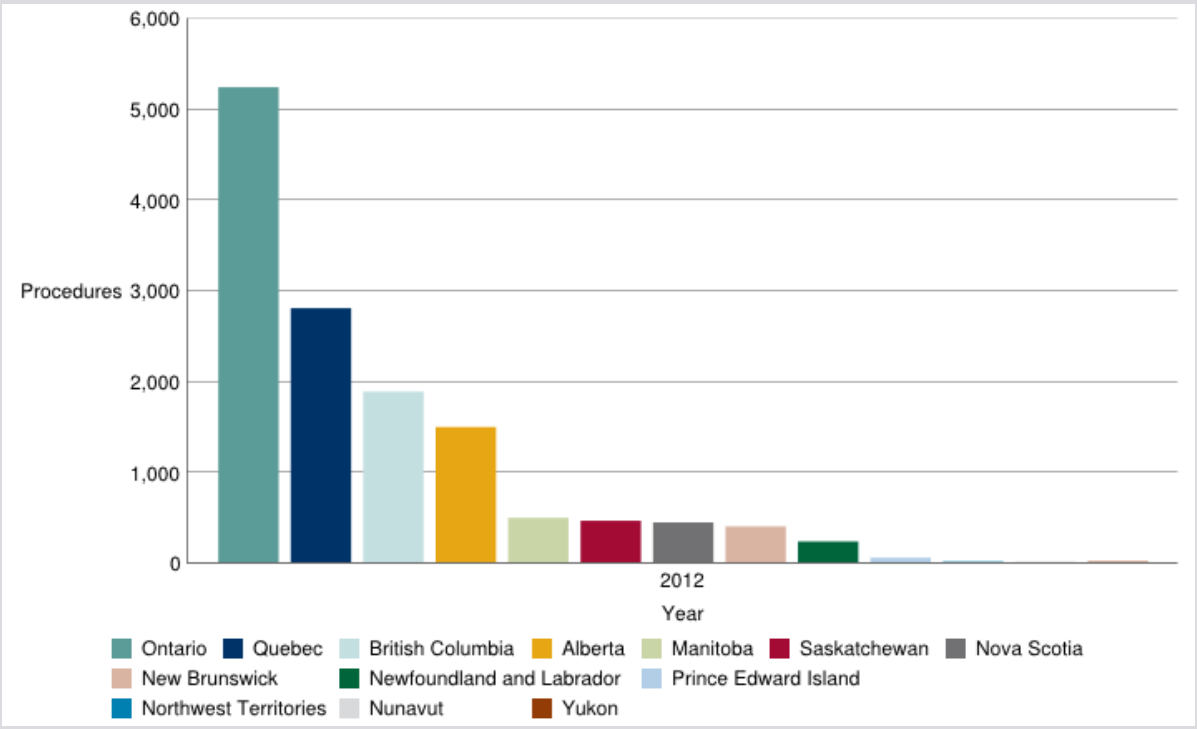
# IMPORTED SURGICAL ALLOGRAFT AND ADM PROCEDURES BY PROVINCE/TERRITORY

The distribution of imported surgical allograft and ADM products across the Canadian provinces and territories varies drastically. The availability and use of these materials is primarily dependent on the province/territory's population, access to domestically available allograft tissue, and presence of sales representatives from the major distributors of these products. Provinces such as Ontario, Quebec, British Columbia, and Alberta have the best access to these products—and thus account for the highest proportion of allograft and ADM procedures—due to the provinces' size and subsequent presence of large hospital centers and regional tissue banks. Because the presence of sales representatives from the leading competitors of imported allografts and ADMs is limited across the country due to the small size of the overall Canadian market, sales representatives who are in the country focus on the large city centers, such as Toronto and Ottawa. This enables them to maximize sales without increasing the costs that would be associated with traveling to all hospitals across the country.

Traditionally, hospitals work independently of each other when buying materials, devices, and supplies from distributors and/or manufacturers. However, to deal with expanding health care costs and restrictive budgets, hospitals are increasingly looking to group purchasing. This involves a group of health care facilities leveraging their collective purchasing power to negotiate a contract to purchase a variety of items at a discount rate from a select number of manufacturers. Known as the tendering process, one of the key advantages of this approach is that the group purchasing organization (GPO) is able to negotiate a price point that generally is lower than the list price of medical devices. An advantage from the manufacturer standpoint is that typical tenders stipulate a prespecified volume be purchased within a particular time period in order for the hospitals in the GPO to get the highest rebates for the products purchased. This provides a guaranteed revenue minimum for those manufacturers that do win the tenders in the bidding process.

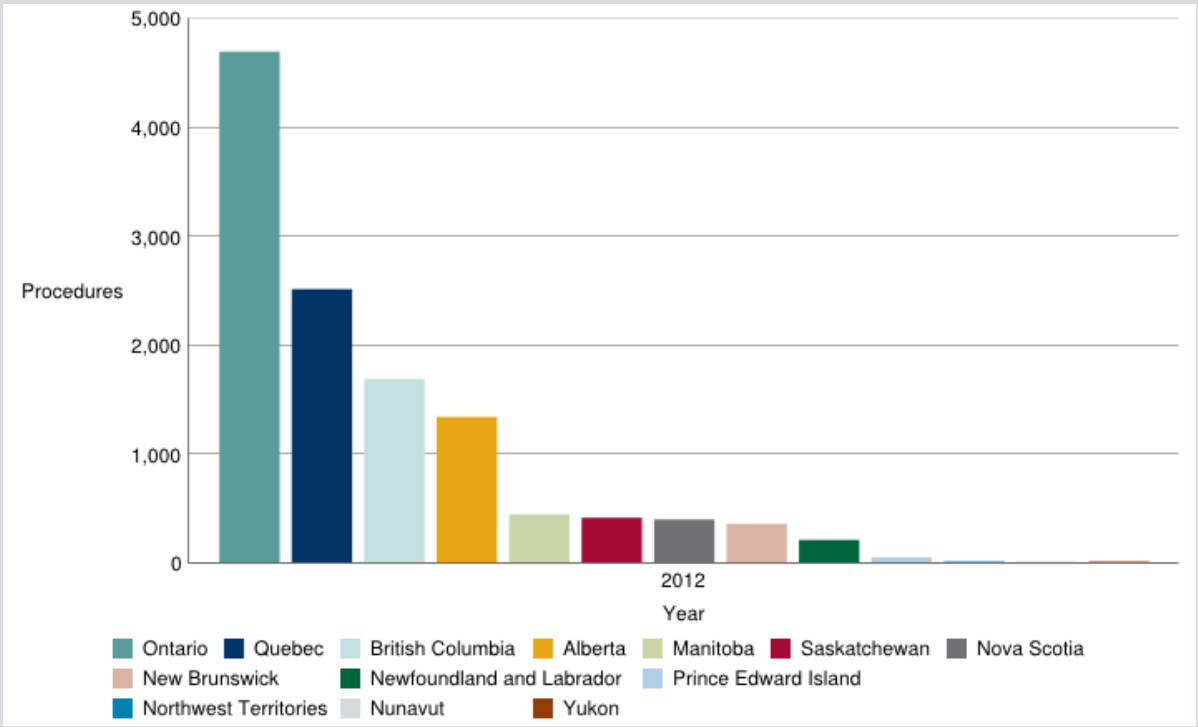
Industry sources have indicated that the tendering process in some provinces will help facilitate the use of allografts and ADMs, as well as make the Canadian market somewhat more attractive to manufacturers outside of the country. For example, British Columbia could potentially negotiate one tender for the entire province, meaning that a single vendor or group of vendors will provide all product needs to all facilities in British Columbia. As a result, facilities in the province would be able to purchase allografts and ADMs at a far lower price than the market average; however, these facilities will only be able to buy the products in question from the manufacturers that are on the tender. This could make the Canadian market more attractive to some competitors because the tendering contracts will secure purchases from multiple facilities, thereby helping to alleviate the challenges of deploying sales representatives to target individual customers scattered across the country. Once the tendering contracts are in place, however, it will also mean that other competitors will not be able to compete in that market for the length of the contract, which will result in decreased competition. Overall, the shift toward tendering will facilitate slight revenue growth in the imported allograft and high double-digit growth in the ADM market over the forecast period and will also significantly impact competitive shares in this space. Industry sources have stated that over the forecast period, Quebec could offer three tenders for the entire province, while in Ontario, there could be upwards of nine tenders.

**Figure 2: Imported Surgical Musculoskeletal and Soft Tissue Allograft and ADM Procedures, by Province/Territory, Canada, 2012**



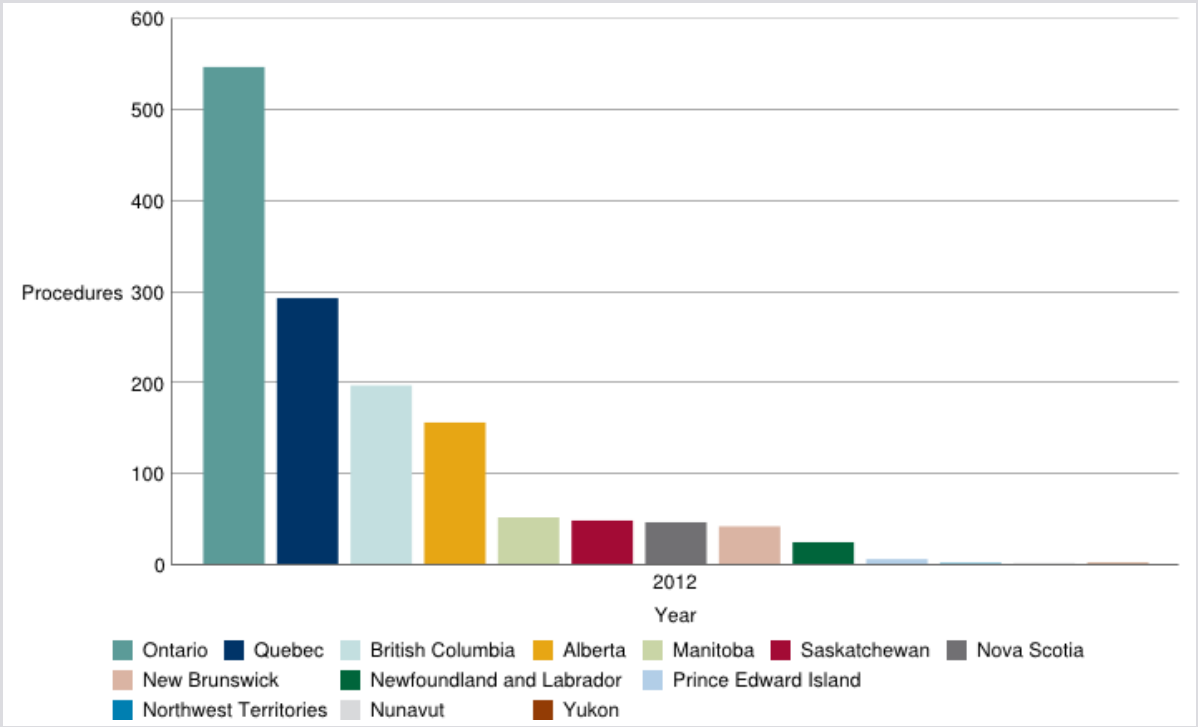

Source: Millennium Research Group

**Figure 3: Imported Surgical Musculoskeletal and Soft Tissue Allograft Procedures, by Province/Territory, Canada, 2012**




Source: Millennium Research Group

**Figure 4: Imported Surgical ADM Procedures, by Province/Territory, Canada, 2012**

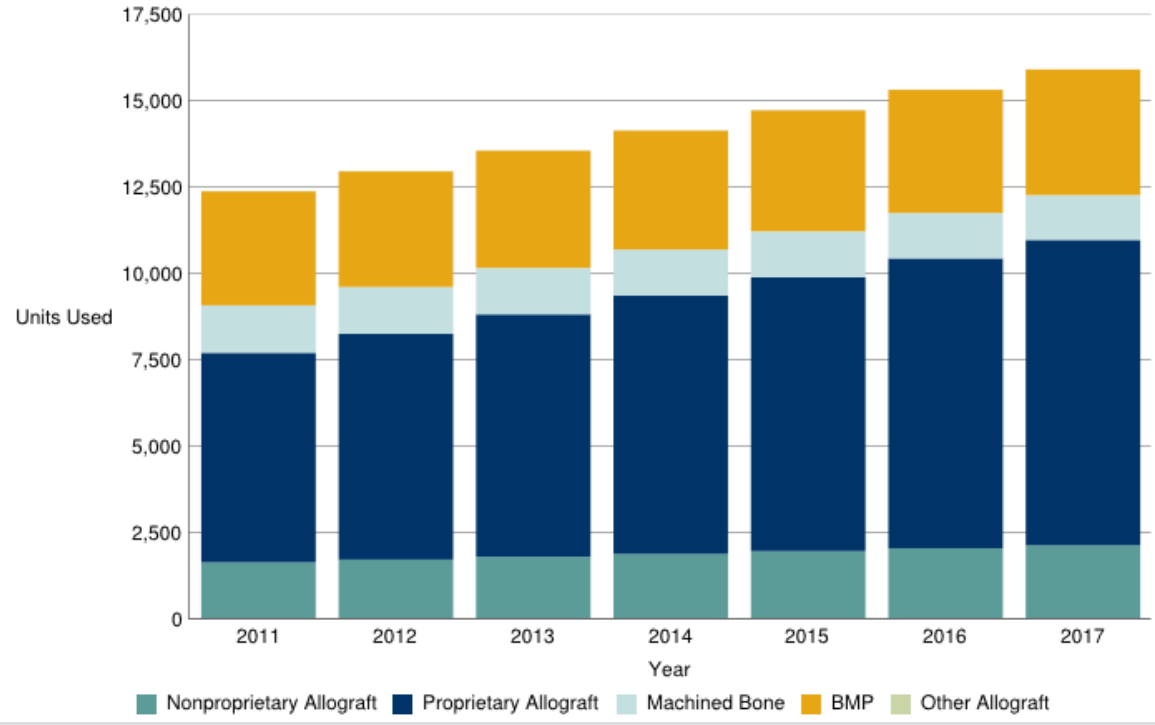



Source: Millennium Research Group

# IMPORTED SURGICAL ALLOGRAFT UNITS BY MATERIAL

Compared to imported BGS market, defined as xenograft and synthetic bone material, imported allograft unit volumes in Canada are small. This is due to a number of reasons. Firstly, almost all imported allograft tissue comes from the US (one provider is located in France). Industry sources have indicated that most US tissue banks and companies that provide tissue to Canada directly give the US first priority for their tissue because they do not have partnerships with companies within Canada, such as RTI Biologics and DePuy (please note that although Synthes and DePuy are subsidiaries of Johnson & Johnson and currently coexist as a joint DePuy Synthes brand, for the purpose of this study, DePuy and Synthes are treated as separate entities). As a result, these companies and tissue banks only provide tissue to Canada if it is requested specifically, if they have sufficient quantities of material, or if a material has been on the shelf for a long period of time. Although some US tissue banks have a larger presence in Canada through wide distribution networks and partnerships with medical device companies, they indicate that the market in the country is very small. This is because nonproprietary hard tissue allografts (except for DBMs) are for the most part available through regional tissue banks in Canada. Furthermore, due to the lower price of domestically sourced allografts, surgeons and hospitals often attempt to utilize these products instead of importing allograft tissue in order to abide by the restrictive hospital budgets. One way surgeons utilize domestic sources is to take other pieces of nonproprietary allograft bone and cut it or chop it themselves to remain cost effective in light of restrictive hospital budgets; however, the availability of nonproprietary soft tissue allografts is limited and requires importation, especially when the patient's own tissue is of subpar quality or the physician foregoes the use of autologous materials during the procedure. Although the limited supply of domestic allograft tissue does make it challenging for Canadian surgeons to rely solely on domestic tissue banks, the relative number of procedures requiring the use of allografts is small compared to the US, curbing Canadian surgeon demand for imported tissue. Also, there are alternatives available to surgeons, such as autografts and BGS, use of which will limit the number of imported allograft units sold in Canada through 2017.

**Figure 5: Imported Surgical Musculoskeletal and Soft Tissue Allograft Units Used, by Material, Canada, 2011–2017**




Notes: Other allografts include other osteobiologics such as allograft dura.

Source: Millennium Research Group

## NONPROPRIETARY ALLOGRAFT UNITS

Nonproprietary allografts such as cortical bone, meniscus, fascia lata, and Achilles tendon that are imported into Canada accounted for the third-largest portion of overall allograft units imported into the country. That being said, Canadian surgeons do continue to look toward domestic supplies and alternatives when nonproprietary allografts are not available. For example, a surgeon may request a femoral head that is unavailable, but other forms of bone, such as a distal shaft, may be available instead. Using alternatives to nonproprietary allografts, however, relies on the tissue bank to inform the surgeon (or purchaser) of these options, which does not always occur. There is also an overall low supply of nonproprietary allograft in Canada that is primarily due to the lack of an organized tissue system. Across the country, there is a lack of integration between the various donor programs in each province or territory; industry sources indicate that the retrieval and processing systems are somewhat disorganized and that tissue is often lost or not harvested because of this. This factor thus limits the availability of domestic nonproprietary allografts and thus requires surgeons to request tissue that needs to be purchased from outside the country. The import of nonproprietary allografts will, however, begin to slow because more organizations, such as Canadian Blood Services, the Trillium Gift of Life Network, and others, expand their efforts to advance public awareness and the increase in the identification, recovery, processing, and distribution of allografts. Furthermore, local tissue banks will increase their efforts to work directly with hospitals and surgeons to ensure that there is better access and awareness of locally available tissue. As a result, imported nonproprietary allograft unit volumes will only expand moderately over the forecast period.

## PROPRIETARY ALLOGRAFT UNITS

Proprietary allografts such as DBMs and cancellous chips and blocks make up a large portion of total imported allograft units in Canada. The majority of these units are accounted for by DBMs because there are few cancellous or corticocancellous chips, powders, and granules imported into the country. This is because it is very simple for a Canadian tissue bank or a surgeon to take whole bone (sourced domestically) and to cut it up into cancellous or corticocancellous chips or granules; therefore, many of these physicians do not feel it is necessary to purchase proprietary allograft chips from an imported source, even though these providers offer the materials packaged in specific sizes. Many surgeons do, however, favor the use of DBMs due to the material's easier handling characteristics in comparison to both proprietary and nonproprietary allografts. The popularity of DBMs has resulted in the material being more heavily marketed in Canada by medical device companies such as Synthes and Wright Medical Technology. In Canada, most imported proprietary allograft chips and nonproprietary allografts are sold through US tissue banks, such as the Musculoskeletal Transplant Foundation (MTF), which predominantly sell their products as requested by customers in the Canadian market.

Industry sources indicate that there continue to be rumors that a domestic company could potentially manufacture and distribute locally made DBMs in the near future. The presence of a domestic bank that offers a DBM will limit the imported DBM market to some extent over the forecast period because the locally produced product will be likely sold at a reduced price due to lower overhead costs and the lack of other associated import expenses that are factored into foreign-produced products. But such an event has yet to materialize. Because DBMs can sometimes be classified as medical devices, they may require adherence to a stringent and costly approval process, which has continued to deter local distributors from entering the DBM space. Through 2017, proprietary allografts will thus continue to account for the largest portion of total imported allograft units in Canada.

## MACHINED BONE UNITS

In Canada, all machined bone allografts sold are manufactured exclusively outside of the country. The units of machined bone allograft sold are one of the lowest of all allograft segments due to the higher pricing associated with purchasing the product from an imported source. The high costs associated with machined bone allograft are especially unattractive when compared to the low pricing and domestic availability of nonproprietary allograft wedges and bone, which can be cut into the appropriate shape required. Also, interbody devices (IBDs) composed of alternative materials, such as titanium and polyetheretherketone (PEEK), are commonly available in Canada at lower prices than machined bone allografts, and surgeons prefer to use these devices in spinal fusions for their radiolucency and strength. Consequently, machined bone allograft units will continue to decline over the forecast period due to the continued increase toward surgeon use of alternative materials and domestic tissue.

## BONE MORPHOGENETIC PROTEIN UNITS

For the purpose of this report, the BMP category consists of Stryker/Olympus' Osteogenic Protein-1 (OP-1), Medtronic Spinal and Biologics' INFUSE, and Biomimetic Therapeutics' Augment. Although Wright Medical Technology was in the process of acquiring Biomimetic Therapeutics as of December 2012, for the purpose of this report, the Augment product is attributed to Biomimetic Therapeutics.

OP-1 is indicated for long-bone nonunions, INFUSE is indicated for lumbar fusions, and Augment is indicated for the foot and ankle. As far as the research indicates, in Canada, OP-1 is still being sold by Stryker with this responsibility anticipated to shift to Olympus at some point during the forecast period. OP-1 and INFUSE have been well received in the Canadian market because of their osteogenic properties and due to strong marketing by the two companies that offer these products. The primary limiter of BMP unit growth overall in Canada is the high cost of this type of allograft, especially in comparison to less expensive BGS and autograft tissue, which are harvested from patients' bodies. Because many Canadian hospitals must operate within strict budgets, purchasing higher-priced products such as BMPs is often unfeasible. As a result, if less costly options are available, BMPs are only approved by the hospital if a surgeon has made a case for their use—typically cases involving older patients with poor bone quality or when the patient is willing to pay for the product themselves.

BMP unit volumes in Canada experienced a decline from 2009 to 2011 stemming from the lawsuits being filed in the US against Medtronic Spinal and Biologics' INFUSE, which resulted from the off-label usage of the product that allegedly resulted in complications. Despite the fact that this was in the US, these lawsuits also negatively impacted INFUSE's sales in Canada, resulting in a drop in total BMP units during that period. That being said, throughout the forecast period, BMP units will experience incremental increases as the negative impact of INFUSE's legal issues starts to subside.

### OTHER ALLOGRAFT UNITS

In this report, other allograft units include allograft-based dura. The allograft-based dura market consists of autologous grafts derived from cadaveric grafts that are sourced from donor specimens and processed for sterilization. Unit volumes will continue to decline throughout the forecast period due to the increasing preference for synthetic alternatives. These competing products are more convenient, cost effective, and easier to apply compared to allograft-based dura. Additionally, by using synthetic products, the chances for disease transmission are eliminated.

The total number of imported allograft units sold in Canada does not include fresh grafts, such as osteoarticular or osteochondral grafts or dura mater. Fresh grafts are not imported because these products must be harvested and implanted within a short period of time. This is extremely difficult to do when the material has to be shipped from outside of Canada; therefore, fresh grafts make up a nominal portion of the imported allograft market. Additionally, industry sources indicate that very few surgeons in the country specialize in procedures involving fresh grafts and demand for these allografts is therefore very low.

Other potential products in the other imported allograft category include orthopedic stem cell products, such as NuVasive's Osteocel and Orthofix's Trinity Evolution, which are available in the US. As of 2012, however, these products were not available in Canada and are not expected to enter the market over the forecast period. Orthopedic stem cell products are therefore excluded from this report. For more information on orthopedic stem cell products, please refer to the introduction chapter.

## IMPORTED SURGICAL ADM UNITS

For the purposes of this report, the ADM market includes allograft-based ADMs used for breast reconstruction and reinforcement grafts used in a variety of general orthopedic, CMF, and sports medicine procedures.

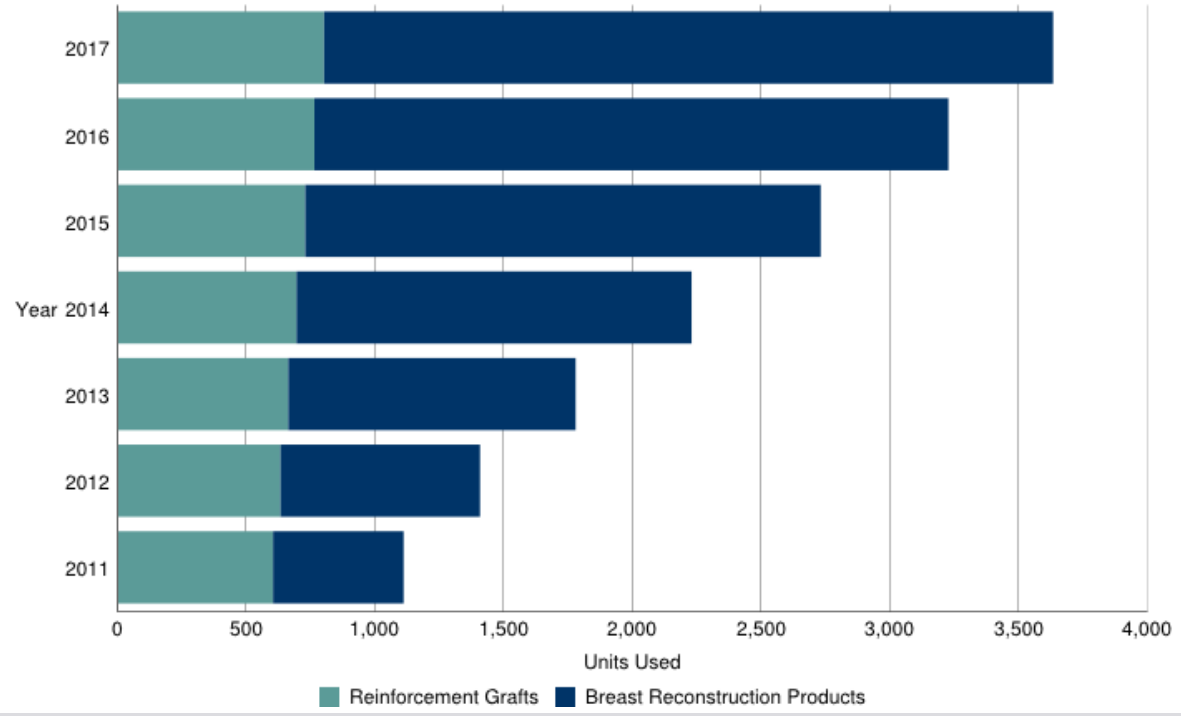
ADMs are composed of cadaver tissue, and its substitutes can be composed of either xenograft or synthetic materials; as previously mentioned, however, the latter two materials are not included in the ADM segment for the purposes of this report. Allograft-based ADMs are used predominantly in breast reconstruction by plastic surgeons because of their laxity, ability to stretch, and ability to provide a more natural look compared to all other types of ADMs. The use of allograft-based ADMs by general surgeons and urologists in procedures like hernia repair is minimal, with these end users preferring xenograft or synthetic products. Consequently, for the purpose of this report, allograft-based ADM market includes only those utilized in the breast reconstruction, which are attributed under the plastic surgeon category, and reinforcement grafts, which are used in a variety of general orthopedic, CMF, and sports medicine procedures.

The first two allograft-based ADMs used in breast reconstruction became available in Canada in early 2009. These were Synthes' DermaMatrix and LifeCell's AlloDerm, which are both composed of cadaver skin tissue. In 2010, C. R. Bard (via its subsidiary Davol) followed suit and introduced the ALLOMAX product to the market. Because all of these products offer a more natural alternative compared to synthetic- or animal-based products, unit growth in the ADM segment will be significantly higher compared to the allograft market as surgeons increasingly adopt these products. All three companies will continue to increase their presence across the country over the forecast period in order to promote their products and expand their revenues, thus leading to robust growth in unit volumes through 2017. As of December 2012, BIOMET's DermaSpan and Arthrex's DermaCell were either not available for sale in Canada and/or not being utilized for the application types covered in this study.

The most popular allograft-based reinforcement graft is Wright Medical Technology's GRAFTJACKET. In general, when a reinforcement graft is used, it is most often an allograft-based graft. Synthetic and xenograft reinforcement grafts (which have not been included in the quantitative outputs of this study) are also available, but some surgeons dislike using these materials because synthetics do not resorb, and xenografts are associated with the potential risk for disease transmission. Another reason contributing to the high popularity of allograft-based reinforcement grafts over xenograft and synthetics is also due primarily to the leading competitor Wright Medical Technology's focus on promoting and marketing its product among its large client base of sports medicine surgeons. Albeit to a lesser extent, allograft-based reinforcement grafts are also used in a variety of CMF and general orthopedic procedures, which are also included quantitatively in this study.

There are, however, other applications for ADM-based products in the US market that are not currently in the Canadian market, most notably ulcer repairs and other forms of tendon repair, such as in the achilles, wrist and elbow, and foot and ankle. The Canadian market for products such as the GRAFTJACKET—and the introduction of additional applications—often strongly lags behind that of the US. This is largely due to the high cost of these products, which is compounded by the smaller budgets of Canadian hospitals. Nonetheless, some of those in the industry expect that the market for ulcer repair in particular could represent a strong opportunity for the reinforcement graft market in the future. However, because the approval and entry of these products into the Canadian ADM market is not currently known at this time, the market models do not include these applications in the ADM segment over the forecast period.

**Figure 6: Imported Surgical ADM Units Used, by Product Type, Canada, 2011–2017**




Notes: Reinforcement grafts are used in general orthopedic, sports medicine, and CMF procedures. Breast reconstruction products include allograft-based ADMs used in breast reconstruction procedures performed by plastic surgeons only.

Source: Millennium Research Group

# IMPORTED SURGICAL ALLOGRAFT AND ADM MARKET BY APPLICATION

In 2012, the general orthopedics market accounted for the vast majority of imported allograft and ADM revenues earned in Canada. This is due mostly to the large number of orthopedic surgeries performed—such as spinal fusions and reconstructive joint replacements—that utilize these materials. In fact, because spinal fusions are performed by both general orthopedic surgeons and neurosurgeons, spinal fusion volumes act as a driver of both application markets. Also contributing to the high revenues earned in the general orthopedics segment is the high price point associated with some of the newer available materials, such as BMPs, machined bone allografts, and DBMs. Many orthopedic surgeons frequently use these materials because a number of the manufacturers of these products are orthopedic device companies and often target their promotional efforts to this specialty. This will be bolstered by the ongoing release of new, high-priced products and surgeon willingness to adopt various allografts. Furthermore, general orthopedics procedures often require larger amounts of graft material compared to the other applications covered in this report. As a result, the general orthopedics segment will continue to be the largest market in Canada through 2017.

As mentioned above, a large number of competitors in the imported allograft market, as well as the reinforcement graft segment of the ADM market, are orthopedic focused. Most of the leading competitors, such as Medtronic Spinal and Biologics, Synthes, Stryker, and Wright Medical Technology,

have a strong presence in the general orthopedics and spine industries in Canada. As such, these companies are able to bundle their hardware and implants with their biologics in order to increase sales and boost market share. Consequently, companies have invested more resources to provide greater awareness, training, and education among surgeons in this space. The general orthopedics segment will therefore continue to be the largest application market in terms of revenues through 2017. At the same time, however, the Canadian biologics market as a whole still remains a considerably underpenetrated in contrast to the US. Many industry sources indicate that most of these companies' sales representatives do not focus heavily on promoting their biologic products, but more on the hardware due to the higher commissions associated with the latter products. While it is possible to bundle both types of products together, many salespeople still focus on selling items that have a higher profit margin, such as spinal fusion or total reconstructive joint implants. As a result, even with the large number of companies in the general orthopedic market, the focus on the imported allograft market as a whole remains somewhat low.

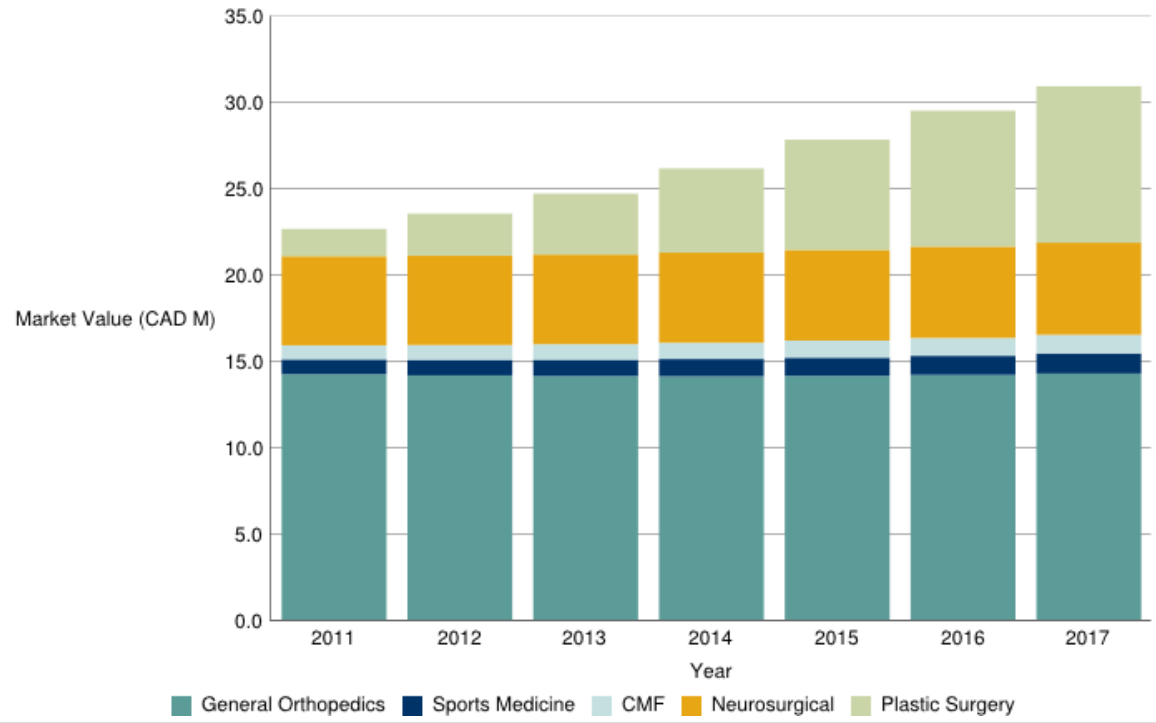
The ADM market, which includes allograft-based ADMs for breast reconstruction and reinforcement grafts used in various applications, is primarily driven by demand among plastic surgeons. This is because allograft-based ADMs are predominantly used in breast reconstruction. With the increased awareness of the advantages of obtaining early breast cancer diagnosis leading to a potentially greater number of mastectomies/lumpectomies and breast reconstructions performed, the market for allograft-based ADMs will continue to experience high growth. Additionally, plastic surgeons will continue to prefer allograft-based ADMs due to their laxity, ability to stretch, and ability to provide a more natural look compared to all other types of ADMs. This being said, like other segments, growth in the ADM market will be somewhat limited due to tight hospital budget constraints and the increasing availability and popularity of BGS-based ADMs, especially synthetic-based ADMs. Nevertheless, the high growth of allograft-based ADMs will allow the plastic surgeon application to maintain the fastest growth through 2017.

The Canadian market for imported allografts and reinforcement grafts used in sports medicine is one of the smaller markets in the country because of the lower number of sports medicine procedures that utilize these materials. While sports medicine physicians do use allografts and reinforcement grafts, there is generally a sufficient amount available from domestic tissue banks. Nonetheless, imported unit sales will be sustained by the high number of procedures requiring nonproprietary allografts, such as rotator cuff reinforcement. As a result, the sports medicine segment will recognize the second-fastest revenue growth in the Canadian surgical imported allograft and ADM market through 2017.

Revenues for imported allografts and reinforcement grafts used in CMF applications were the lowest in Canada in 2012. Only a small number of CMF procedures performed in the country use these materials; in most procedures, autograft is used instead. Overall ASPs for materials in this application are also not as high as other applications because often, a lower volume of tissue is required for CMF procedures. Furthermore, the vast majority of procedures performed by CMF surgeons are caused by trauma or tumors. Because only a finite number of trauma and tumor cases occur each year, no significant changes will occur in terms of unit sales or revenue growth over the forecast period. Market expansion will, however, occur due to the aging demographic in Canada. As individuals grow older, the risk of accidents and falls increases. Additionally, with age comes with the associated higher incidence of cancer. The aging Canadian population will thus contribute to the need for CMF surgeries, some of which will require the use of allografts and reinforcement grafts. This driver will, however, be somewhat countered by ongoing public campaigns to raise awareness of the signs and symptoms of cancers, aneurysms, and other diseases, which will enable earlier diagnosis and treatment, sometimes eliminating the need for surgery and thus the materials used in these procedures.

The neurosurgical segment accounted for the second-largest amount of imported allograft and ADM revenues in 2012, mainly due to the high number of spinal fusions and dural repairs performed that commonly use these materials. Imported tissue is more often used in spinal fusions and dural repairs compared to nearly all other applications because the products often used in these procedures—such as allograft chips and a wide range of other products, such as DBMs and BMPs—are only available through importation. Nevertheless, neurosurgical applications will exhibit the second-lowest revenue growth through 2017 because neurosurgery volumes, especially spinal fusions, are growing only modestly. Furthermore, due to budgetary pressures, many neurosurgeons are forced to opt for alternatives, such as autograft and domestically available allograft tissue.

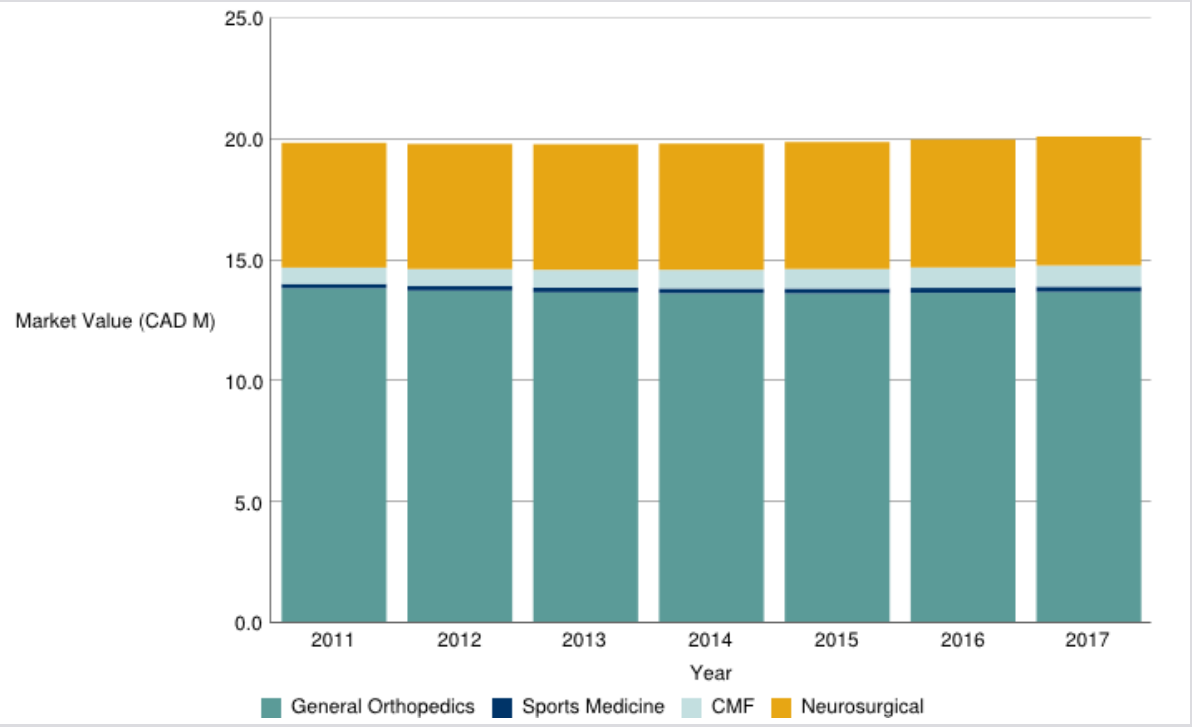
**Figure 7: Imported Surgical Musculoskeletal and Soft Tissue Allograft and ADM Market, by Application, Canada (CAD), 2011–2017**




Notes: (1) General orthopedics include general orthopedic surgeons, orthopedic spine surgeons, trauma surgeons, and general surgeons. (2) ADMs include reinforcement grafts used in general orthopedic, sports medicine, and CMF procedures, as well as allograft-based ADMs used in breast reconstruction procedures (plastic surgery).

Source: Millennium Research Group

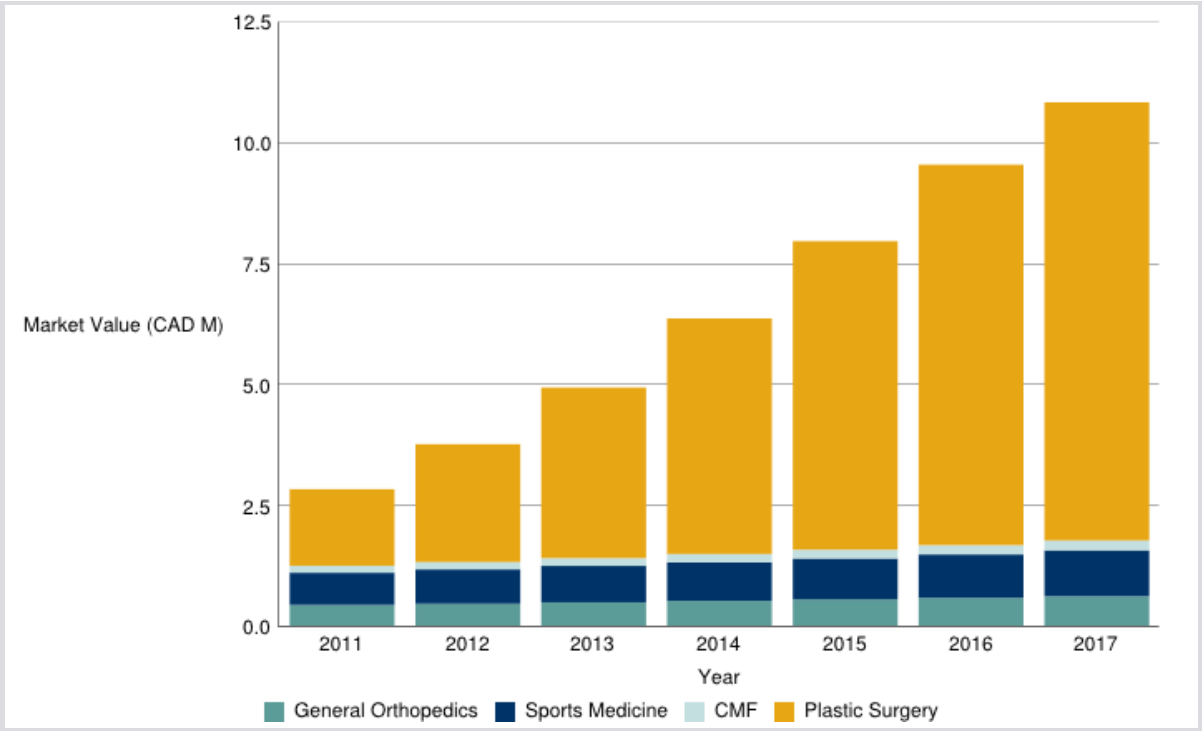
**Figure 8: Imported Surgical Musculoskeletal and Soft Tissue Allograft Market, by Application, Canada (CAD), 2011–2017**




Notes: General orthopedics include general orthopedic surgeons, orthopedic spine surgeons, trauma surgeons, and general surgeons.

Source: Millennium Research Group

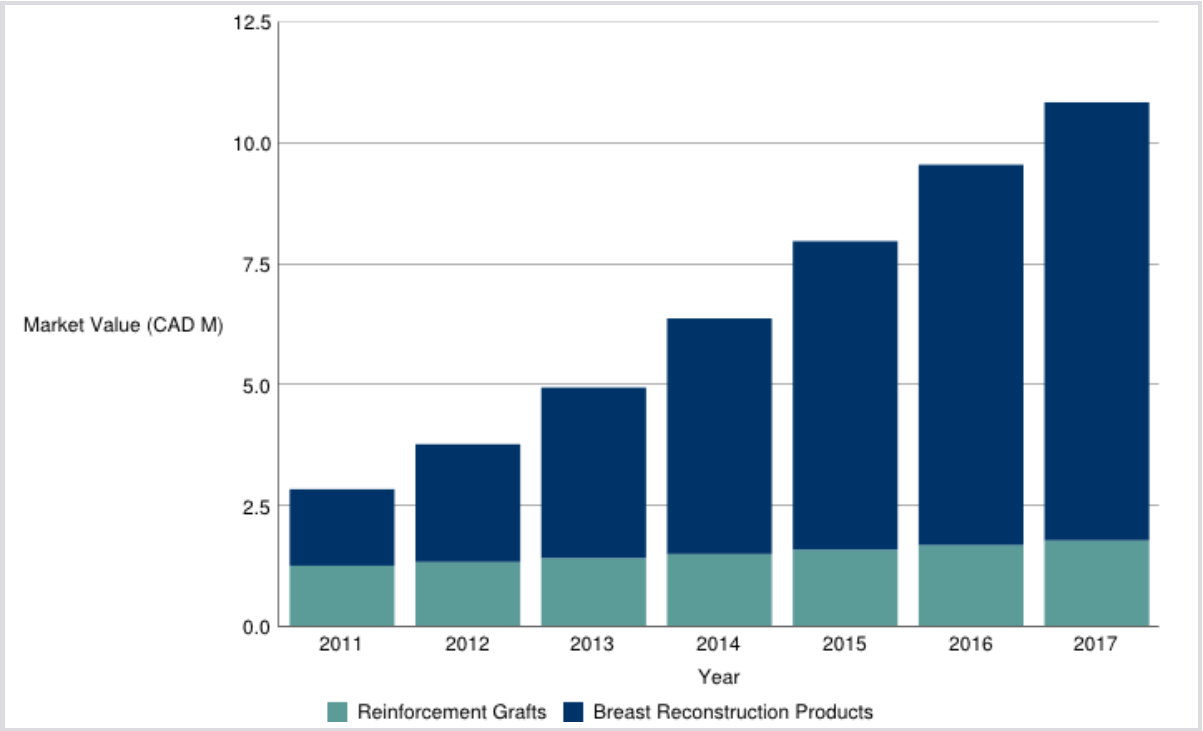
**Figure 9: Imported Surgical ADM Market, by Application, Canada (CAD), 2011–2017**




Notes: (1) General orthopedics include general orthopedic surgeons, orthopedic spine surgeons, trauma surgeons, and general surgeons. (2) ADMs include reinforcement grafts used in general orthopedic, sports medicine, and CMF procedures, as well as allograft-based ADMs used in breast reconstruction procedures (plastic surgery).

Source: Millennium Research Group

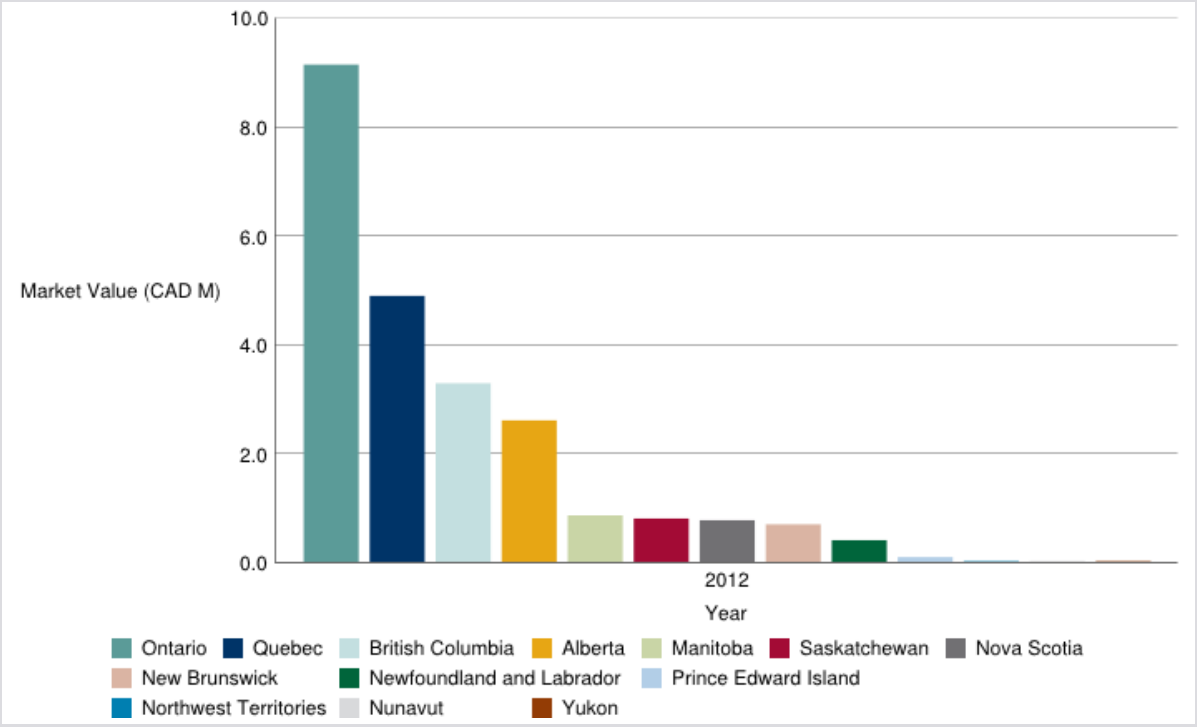
**Figure 10: Imported Surgical ADM Market, by Product Type, Canada (CAD), 2011–2017**




Notes: Reinforcement grafts are used in general orthopedic, sports medicine, and CMF procedures. Breast reconstruction products include allograft-based ADMs used in breast reconstruction procedures performed by plastic surgeons only.

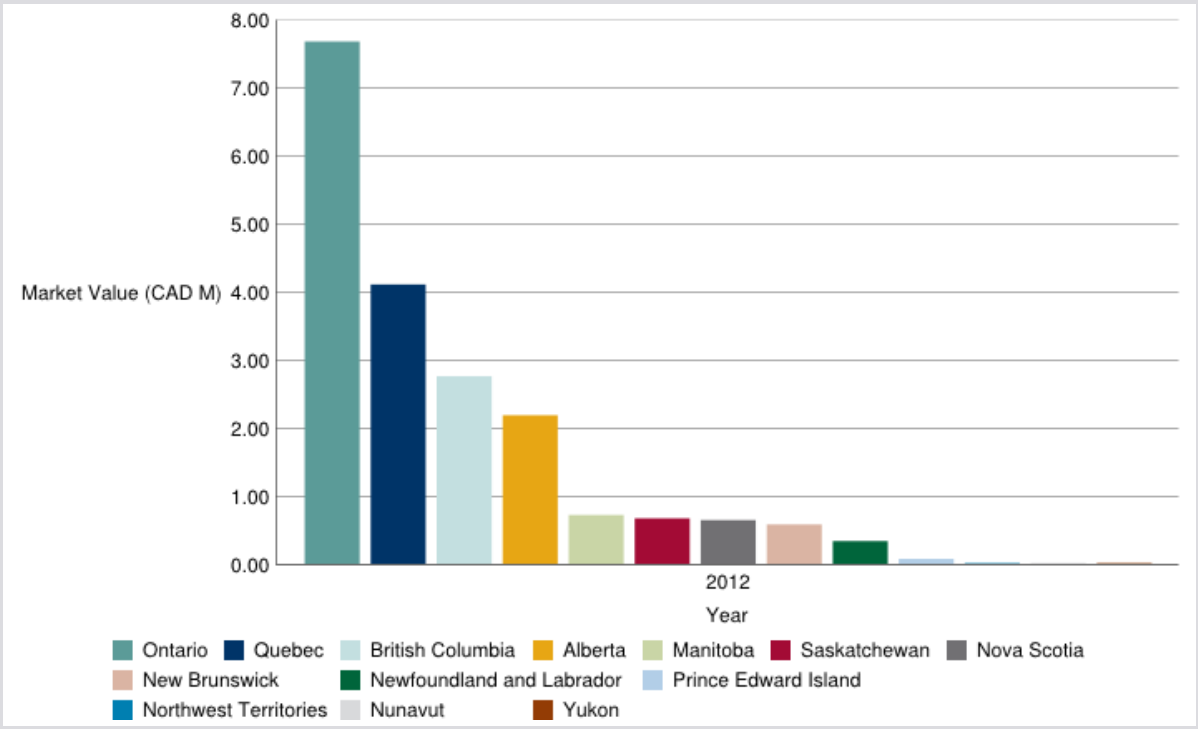
Source: Millennium Research Group

**Figure 11: Imported Surgical Musculoskeletal and Soft Tissue Allograft and ADM Market, by Province/Territory, Canada (CAD), 2012**



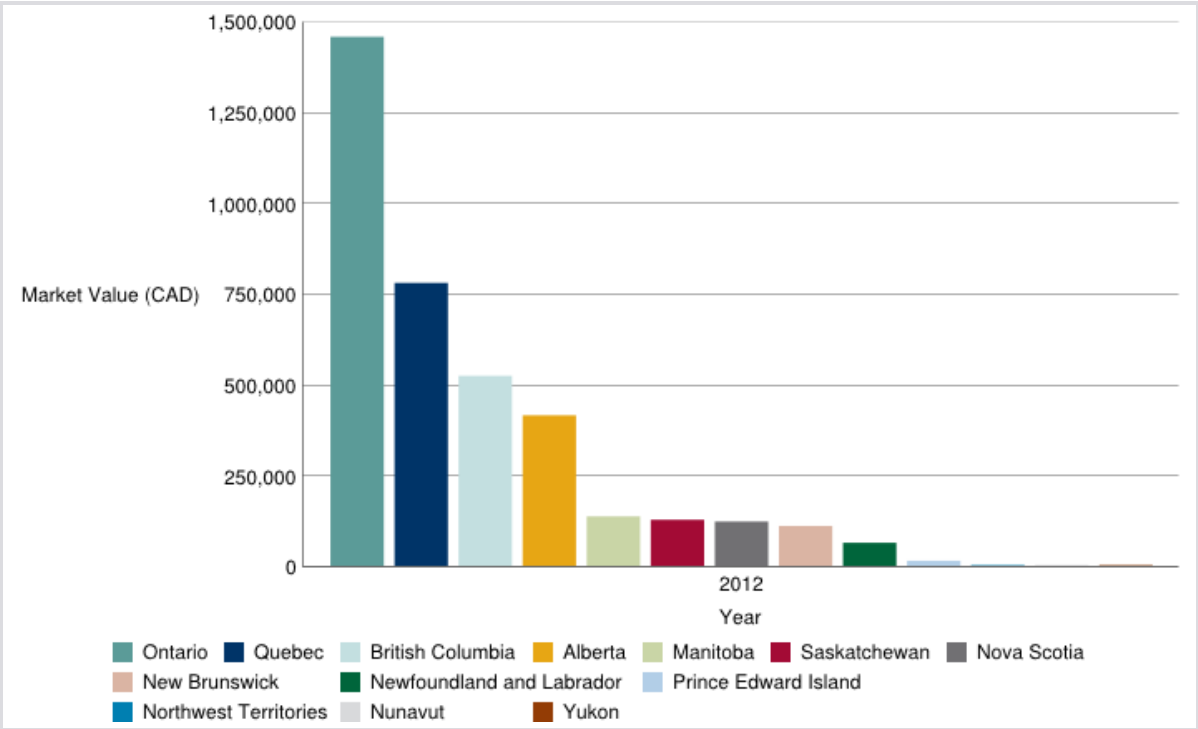

Source: Millennium Research Group

**Figure 12: Imported Surgical Musculoskeletal and Soft Tissue Allograft Market, by Province/Territory, Canada (CAD), 2012**




Source: Millennium Research Group

**Figure 13: Imported Surgical ADM Market, by Province/Territory, Canada (CAD), 2012**




Source: Millennium Research Group

# FUTURE INNOVATIONS AND TECHNOLOGICAL ADVANCEMENTS

For the most part, Canadian surgeons seem to have mixed feelings regarding their preferences for using new materials. Choice of material is dependent on a variety of factors that include efficacy, cost, value, availability, learning curve, and product reputation, among other considerations. These factors will continue to influence Canadian surgeons' lukewarm reception to new materials throughout the forecast period.

Below are summaries of some key insights from the 5 Canadian surgeon interviews that were conducted for this study:

- In general, Canadian surgeons have stated they have to function within strict yearly budgets that have been allocated to their respective hospitals. Despite some surgeons having expressed interest in new materials that are generally associated with a higher cost, these surgeons do not have the monetary freedom to utilize them often. Consequently, a large number of Canadian surgeons will continue to request less expensive materials.

- Those that stated they would be potentially interested in a new material indicated that new products that prove to be more efficacious have a good opportunity of being adopted. Surgeons, especially younger ones, are receptive to using new products if the quality of the material is supported by documentation. One orthopedic surgeon was very impressed by the strength and reliability of a synthetic product, whereas another orthopedic spine surgeon continues to use allografts because it represents a "higher-quality" product. Another surgeon claimed that the limited use of BMP was not because of the price, but because of the "the unpredictable nature of the response." All surgeons agreed that the well-being of the patient was the priority and that the effectiveness of the product (which includes many factors such as the product being antiseptic, durable, and having high bone resorption) takes precedence over other factors, including the costs.

- Newer products need to be readily available to physicians. Because hospitals have their own tissue banks, doctors prefer using allografts because they can immediately access the tissue for surgeries. That being said, new products with availability issues are less likely to be adopted by surgeons.

- Manufacturers of advanced products often do not concentrate their resources heavily in Canada because the market opportunity for allografts and ADMs is so small. Because of this, there is limited marketing of and education provided for these products to surgeons, and many are unaware of the materials available.

- Canadian surgeons are distinguished as a small, close-knit community. Because doctors frequently discuss the efficacy of the various products with each other, negative discourse can quickly spread. As a historical case, the reputation of LARS Ligaments' was damaged after a doctor used the product for an improper indication, causing severe harm to the patient. The synthetic product was scrutinized and has struggled to recover its reputation as an efficacious device. Consequently, the reputations that new products initially elicit can often dictate the long-term success or failure of their manufacturers.

- New products that are difficult to work with are less likely to be readily adopted by surgeons. A surgeon who used the synthetic dura product Dura-Gel stopped using it because it was noted

that the product was hard to work with. This demonstrates that physicians will be reluctant to use products they lack training for, particularly products associated with a steep learning curve.

### ORTHOPEDIC STEM CELL PRODUCTS

As of 2012, several orthopedic stem cell products were available in the US, most notably Trinity Evolution (Orthofix) and Osteocel (NuVasive). These products contain mesenchymal stem cells (MSCs), which are commonly found in bone marrow. When tissue is damaged, these cells will travel to the site of tissue injury, at which point they differentiate into the tissue that is needed for the repair. These products rely on marrow-rich cadaver bones, typically vertebrae or long bones, which are harvested from a tissue donor and sent to a manufacturing facility where they are tested for disease and stem cell concentration. The tissue is then processed into an allograft paste and treated to remove any immunogenic cell characteristics. Eliminating these characteristics allows the stem cells to be implanted into any patient without eliciting an immune response. Orthopedic stem cell products can be kept frozen for up to 2 years.

As of December 2012, orthopedic stem cell products were not yet available in Canada and were thus not included in this report; however, it is likely that these products will enter the Canadian imported allograft and ADM market in the next 10 years. Orthopedic stem cell products have been well accepted by many surgeons in the US despite their high price because of their effectiveness in stimulating the formation of new bone. Once these products enter the Canadian market, they will likely be adopted modestly, albeit not as strong as in the US because their use will be severely restricted by their high cost. Much like BMPs, orthopedic stem cell products will likely be saved for high-risk, older patients who will exhibit greater benefits from the addition of these products to their healing process.

## MARKET DRIVERS AND LIMITERS

**Table 1: Drivers and Limiters of the Musculoskeletal and Soft Tissue Imported Surgical Allograft and ADM Market, Canada**

| Market Driver | Market Limiter |
|---|---|
| » Shift away from the use of autografts<br>» Growing surgeon preference for allografts over autografts<br>» Favorable demographics and increasing physical activity<br>» Nationwide tissue system processes<br>» Improved physician training and awareness<br>» Greater variety of DBMs available<br>» Negative publicity regarding xenografts<br>» Increasing adoption of ADMs | » Elevated cost of allograft and hospital cost-containment pressures<br>» Gradual development of Canadian tissue bank structure and organization<br>» Canada's small population relative to its land mass<br>» Continuing emergence of alternative treatments and technologies<br>» Limited need for imported allograft tissue<br>» Concerns regarding disease transmission |
| Source: Millennium Research Group | |

# MARKET DRIVERS

## SHIFT AWAY FROM THE USE OF AUTOGRAFTS

In Canada, many surgeons are becoming increasingly aware of the disadvantages of harvesting autograft bone and soft tissue from patients. In particular, surgeons have raised concerns about the declining quality of bone associated with age, the lengthened recovery times, and the added pain to the patient. Furthermore, the overall cost of a second harvesting procedure—in terms of increased surgeon, operating, and recovery time—sometimes exceeds even the most expensive allograft products. Although autograft bone has historically been the standard of care because of its osteoinductive, osteoconductive, and osteogenic properties, many surgeons are finding alternate methods to acquire the same features with fewer disadvantages. For instance, a number of surgeons are using allograft alone, in combination with autograft, or with bone marrow aspirate (BMA). In soft tissue procedures, the use of autograft requires the surgeon to remove cartilage, tendons, or other soft tissue from the patient's body, in most cases the knee, which can disrupt the stability and strength of the patient's structural support in that joint. Awareness of these limitations and the availability of alternatives are fueling a shift away from the use of autograft to other materials, such as allografts and ADMs. The Canadian market for these products will therefore expand through 2017.

## GROWING SURGEON PREFERENCE FOR ALLOGRAFTS OVER AUTOGRAFTS

Older, more experienced surgeons in Canada are more likely to choose autograft over allograft materials because they were initially trained to use autografts. Many of these surgeons are, however, beginning to retire, and younger surgeons have taken their place. By contrast, younger physicians have received training with newer allograft products and are therefore more willing to use alternatives to autograft, such as DBMs and BMPs. Additionally, competitors have made it a point to increase the marketing of their allograft products to educate and train surgeons on the benefits of using allografts over autografts. These increased efforts by competitors, along with younger surgeons entering the field, will help maintain growth in the number of procedures that use allografts, the majority of which are imported, over the forecast period.

## FAVORABLE DEMOGRAPHICS AND INCREASING PHYSICAL ACTIVITY

Over the forecast period, there will be a growing proportion of individuals over the age of 50 in Canada. This will lead to a subsequent increase in age-related diseases such as osteoporosis and degenerative disc disease (DDD). Rates of osteoporosis, which raises the risk of bone fractures, are rising because of the greater prevalence of risk factors such as poor nutrition from diets that are high in fat and low in vitamin D and calcium. Those who suffer from osteoporosis are more likely to need a bone graft for two reasons. First, fractures among patients with low bone density are typically more severe and more likely to require some sort of bone graft material. Second, surgeons are more reluctant to use autograft when performing an operation on an osteoporotic patient because the condition reduces the quality of the autograft.

As the Canadian population ages, the number of DDD cases will also climb because the disease is primarily caused by the effects of aging on the spine. Due to age, the intervertebral discs can become stiff and rigid, causing pain and other symptoms. Spinal fusions are performed to treat the condition and will therefore increase in volume over the forecast period. Expansion of the elderly demographic in Canada

will thus expand the patient base for treatments requiring allografts and positively impact the market for these materials.

Additionally, the slowly rising rates of diabetes and obesity in Canada will also contribute to allograft-based procedural expansion by heightening the number of patients that require surgery to treat many problems associated with these conditions, such as herniated discs and knee cartilage damage.

In addition, the country's baby boomers are taking part in physical activity more frequently than previous generations; they are increasingly aware of the benefits of maintaining a healthy lifestyle. Greater participation in sports will, however, lead to a higher number of sports-related injuries and will subsequently boost the volume of trauma and soft tissue procedures performed, thereby expanding the use of allografts and contributing to revenue growth over the forecast period.

## NATIONWIDE TISSUE SYSTEM PROCESSES

As of the end of 2012, Canada did not have a nationwide-organized tissue donation system. Because of this, each province or territory acts on its own behalf and is responsible for the recovery, cleaning, and distribution of domestic allograft tissue. Some poor practices have thus developed; for example, at times, tissue is lost or not recovered in time due to a lack of communication and collaboration between all parties involved. Consequently, there is a lag in time between when a patient is ready to donate tissue and when the tissue banks are ready to receive it. Tissue donation itself is low in the country compared to some other developed countries, such as the US, which contributes to considerable demand for imported allografts and ADMs. While there are some attempts within provinces to improve these processes by organizations such as Canadian Blood Services, Trillium Gift of Life Network, and others, there is still a disconnect between the general population knowing and willing to donate their tissue and the ability for it to get harvested and used properly. Due to the lack of a nationwide-controlled tissue donation and distribution program, imported allografts and ADMs will be available alternatives to surgeons when autografts and domestic allografts are not viable options.

## IMPROVED PHYSICIAN TRAINING AND AWARENESS

Competitors in the Canadian market for imported allografts and ADMs for surgical applications have continued to increase their marketing and training efforts to increase the awareness and adoption of their products. Although manufacturers are still cautious about placing a large number of sales reps in Canada because the geographic location of physician and patient populations are sparse, they are still utilizing other avenues (e.g., conferences, seminars, training sessions, newsletters, emails) to educate surgeons on the benefits and efficacy of their allograft and ADM products. For example, enhanced physician training for arthroscopic surgery has driven the adoption of reinforcement grafts in rotator cuff repairs. Furthermore, the increasing market presence of Wright Medical Technology's GRAFTJACKET has boosted physician awareness of the different reinforcement graft options. The GRAFTJACKET has been well presented at conferences and is being used in several studies. Over the forecast period, surgeon training for arthroscopic surgery and awareness of the various reinforcement graft options available will heighten the proportion of physicians who will use reinforcement grafts for relevant procedures, including rotator cuff reinforcement. Imported units will increase as a result.

### GREATER VARIETY OF DBMS AVAILABLE

In order to remain competitive, DBM manufacturers have introduced new allograft products into Canada that provide improved handling characteristics and greater effectiveness. Typically, new DBMs consist of a composite of DBM with cancellous chips or synthetic materials. The benefits of these products will promote surgeon adoption of these materials over autografts. Moreover, their higher price will help offset some of the ASP declines and boost revenue growth over the forecast period.

### NEGATIVE PUBLICITY REGARDING XENOGRAFTS

In an article published in the *Journal of Bone and Joint Surgery*, it was concluded that a large number of patients suffered serious adverse reactions to DePuy's Restore Orthobiologic Implant and that it was not recommended for use in rotator cuff repairs (Walton JR, 2007). Because the product is a porcine-derived product, the publication of the article not only negatively impacted DePuy's sales, but also the entire xenograft market. Due to these findings, many physicians were hesitant to use xenografts due to the fear of an inflammatory reaction in patients. Some of these concerns will linger among surgeons, thereby somewhat limiting sales of imported porcine-derived reinforcement grafts in Canada over the forecast period. This will help fuel the use of other materials, contributing to growth in the imported allograft-based reinforcement graft market through 2017.

### INCREASING ADOPTION OF ADMS

The ADM segment of the Canadian imported allograft and ADM market will continue to experience the highest growth rate over the forecast period. In particular, allograft-based ADMs continue to be the most preferred by plastic surgeons due to the products' laxity, ability to stretch, and ability to provide a more natural look compared to all other types of ADMs. Overall, a rise in allograft-based ADM use, combined with the products' high prices, will help maintain the ADM market's double-digit growth through 2017. The rapid expansion of this segment will thus contribute to revenue increases in the Canadian imported market for allografts and ADMs.

## MARKET LIMITERS

### ELEVATED COST OF IMPORTED ALLOGRAFTS AND HOSPITAL COST-CONTAINMENT PRESSURES

In Canada, hospitals receive a budget from the government that covers their costs over the course of a year. Many hospitals in the country are operating at a deficit and are looking for ways to decrease spending in order to realign their expenses with their budgets. Hospitals are therefore increasingly encouraging surgeons to consider the financial implications of the materials used in surgery. For example, during the global economic downturn, many cost-constrained Canadian hospitals mandated that surgeons use more affordable products, such as domestically available allograft tissue or autografts. These cost-savings practices will continue to be implemented in hospitals over the forecast period. Because a number of physicians will switch to more affordable products, there will be downward pressure on ASPs in the imported allograft market and only minimal increases in ASPs in the ADM segment. The greater adoption of autografts and lower-cost domestically available allografts will also impede the number of imported products sold in Canada through 2017.

Furthermore, industry sources indicate that as tenders become more readily available, it will contribute to the downward pressure on ASPs throughout the forecast period. With British Columbia likely to have one tender and Ontario and Quebec with the potential to have a number of tenders, more products will be purchased in bulk at reduced prices. The ASP for imported allografts will therefore face strong downward pressures, while ADM ASPs will be limited to only nominal increases, resulting in restricted growth of these products over the forecast period.

## GRADUAL DEVELOPMENT OF CANADIAN TISSUE BANK STRUCTURE AND ORGANIZATION

Industry sources have indicated that some of the domestic tissue banks in Canada are working to develop their businesses to be more in line with the US system, which is viewed as being much more sophisticated and developed. Tissue banks are developing improved processes and recovery techniques to improve their supply of tissue. Additionally, tissue banks are working more closely with surgeons and hospitals to understand what types of tissue are needed and to determine alternatives that are just as efficacious when a particular type of tissue is unavailable. For example, more conservative surgeons typically ask for femoral heads because they are accustomed to using them. As a result, when femoral heads are not available, tissue banks need to explain that other types of bone, such as cancellous bone or whole bone shafts, are available instead; they will also need to be able to demonstrate that these alternative materials work just as well. Overall, gradual improvements made to the organization and structure of Canadian tissue banks—via efforts made by organizations such as Canadian Blood Services, Trillium Gift of Life Network, and others—will continue to make it easier for surgeons to obtain allografts locally, which will modestly restrict the number of imported allografts sold in Canada over the forecast period.

## CANADA'S SMALL POPULATION RELATIVE TO ITS LAND MASS

According to the Central Intelligence Agency (CIA) World Factbook, Canada has the second-largest total area, yet its total population is roughly the size of California (Central Intelligence Agency, 2013). Because of this, some companies lack the incentive to fully expand the imported allograft and ADM markets within the country. To operate sales forces outside of the large city centers, companies either have to pay for a significant amount of travel for one sales representative to reach every hospital in each province and territory or hire a large number of people to service various locations across the country. Most competitors in the imported allograft and ADM market in Canada therefore focus only in the large cities and, in some cases, solely in the more heavily populated provinces, such as Ontario, British Columbia, and Alberta. The markets outside of these centers are often considered too small and too costly for the company to reach all of the hospitals in these areas. Consequently, this has resulted in a void of sales reps in the low-population areas outside of the large city centers. This factor has and will continue to limit the Canadian market for imported surgical allografts and ADMs through 2017.

## CONTINUING EMERGENCE OF ALTERNATIVE TREATMENTS AND TECHNOLOGIES

In Canada, the emergence of treatments and technologies that compete with surgical procedures that involve the use allografts will impede overall market growth. For example, spinal nonfusion devices represent an alternative to spinal fusion implants that treat back pain while preserving motion between the vertebrae. By contrast, spinal fusions fuse the vertebral bodies, causing the patient to lose motion at that particular level of the spine. Dynamic stabilization systems and artificial discs are examples of the nonfusion technologies that will become more prevalent in Canada over the forecast period due to their motion-preserving abilities. These technologies do not involve the use of bone graft material, and the

adoption of nonfusion devices will thus limit the imported allograft market, especially because spinal fusions represent the most common application of bone grafts, particularly premium-priced BMPs. Consequently, as spinal fusion volumes are impeded by the growing popularity of nonfusion technologies, the overall imported allograft market in Canada will be negatively affected accordingly.

## LIMITED NEED FOR IMPORTED ALLOGRAFT TISSUE

Although the supply of allograft tissue in Canada can be, at times, significantly low, in order to save costs and work within restrictive hospital budgets, Canadian surgeons will look to alternative material types from local tissue banks before utilizing the import route. Additionally, the overall number of surgical procedures being performed in the country that require the use of the materials is not considerably high, thus limiting sales of and overall revenues for imported allografts and ADMs.

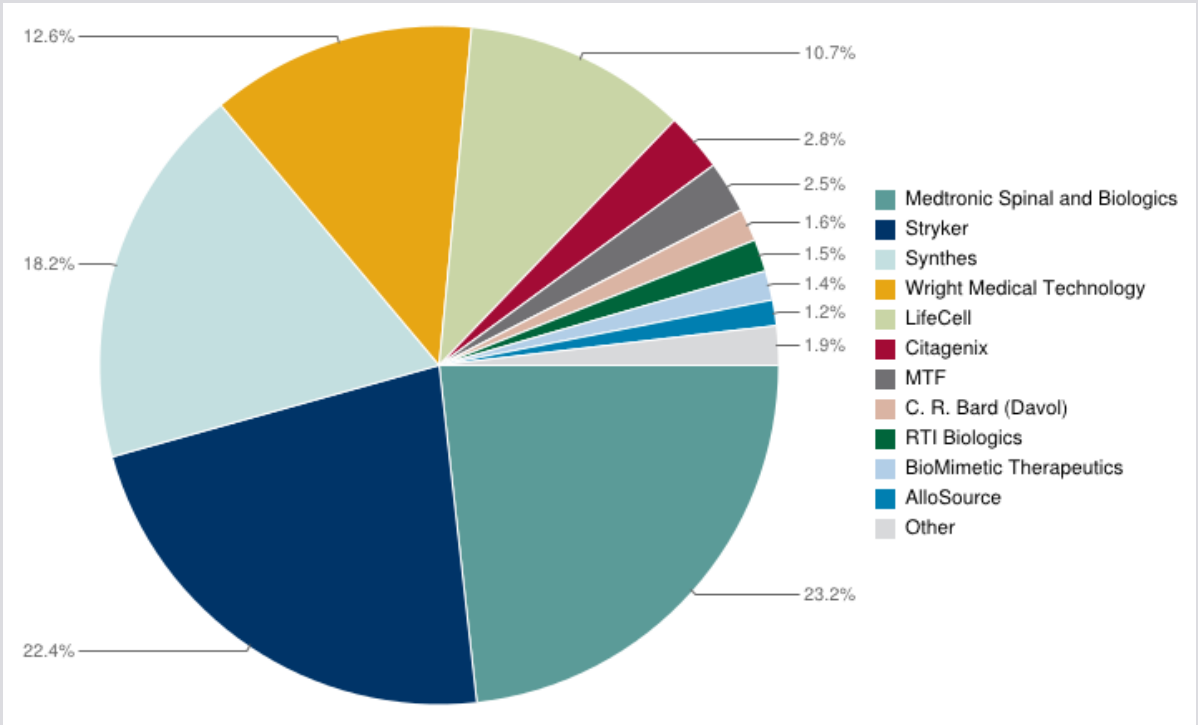
## CONCERNS REGARDING DISEASE TRANSMISSION

A major concern that persists regarding the use of various types of allograft materials is the risk of disease transmission. In response to these concerns, many manufacturers and donor locations have implemented strict processing and handling procedures to ensure the safety of their allograft materials. Companies are using patented cleansing processes to remove antigens and surface lipids. Donors are also thoroughly screened for infectious diseases such as hepatitis and HIV. All of these measures have been implemented to ensure the safety of allografts, which will alleviate patient, clinician, and surgeon fears regarding the use of allografts. As a result, these materials will be increasingly used over the forecast period.

# IMPORTED SURGICAL ALLOGRAFT AND ADM MARKET COMPETITIVE ANALYSIS

The Canadian imported surgical musculoskeletal and soft tissue allograft and ADM market comprises a wide variety of materials for a number of different procedures, which has led to an array of competitors within the market. The major competitors are predominantly medical device companies that have a strong international presence, such as Stryker, Medtronic, or Synthes. Many of the major tissue banks also distribute through exclusive agreements, such as the MTF and Synthes, or through nonexclusive agreements with a variety of companies in Canada, such as AlloSource, which collaborates with Medtronic and Zimmer. In a few cases, foreign competitors distribute solely through Canadian companies, such as Integra LifeSciences, which distributes through Citagenix.

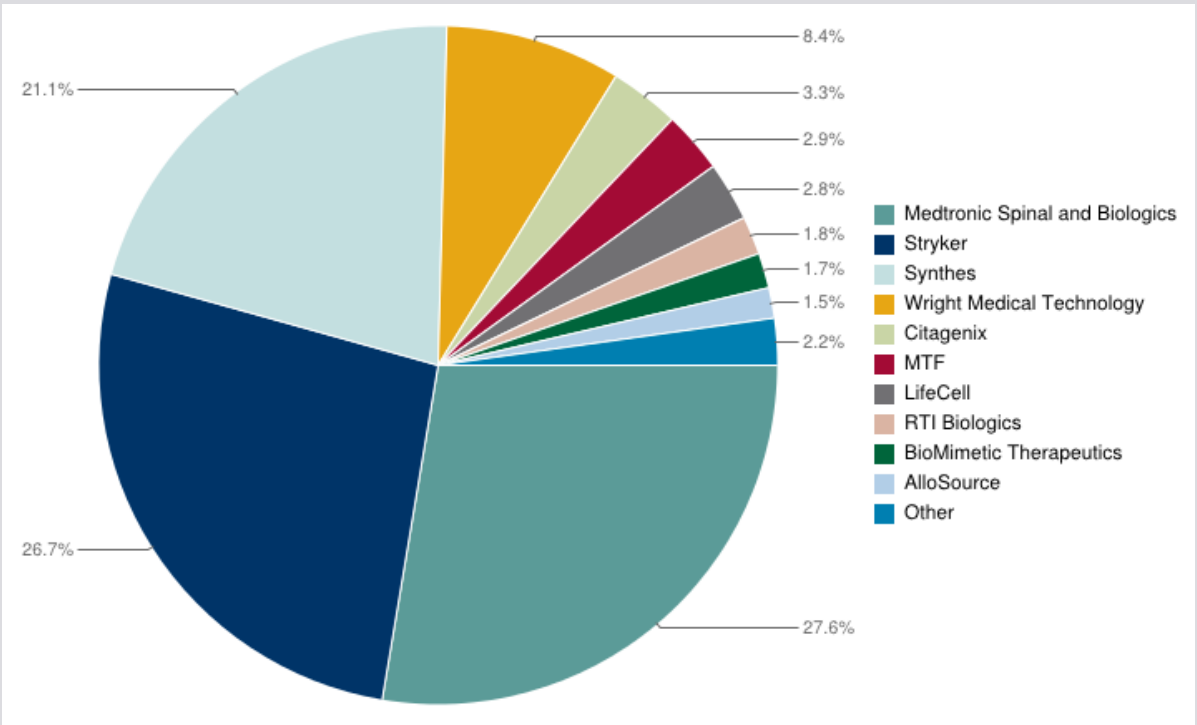
**Figure 14: Leading Competitors in the Imported Surgical Musculoskeletal and Soft Tissue Allograft and ADM Market, as a % of Total, Canada, 2012**




Notes: (1) Numbers reflect rounding. (2) Other includes Arteriocyte Medical Systems, Atrium Medical, Bacterin International, Biomet, Codman & Shurtleff, Community Tissue Services, DePuy, Harvest Technologies, J. K. Orthomedic, LifeLink Tissue Bank, LifeNet Health, pfm medical, Puget Sound Blood Center, RegenMed, Rocky Mountain Tissue Bank, Sorin Group, Synovis Life Technologies, Tissue Bank Manitoba, TissueNet, and Zimmer.

Source: Millennium Research Group

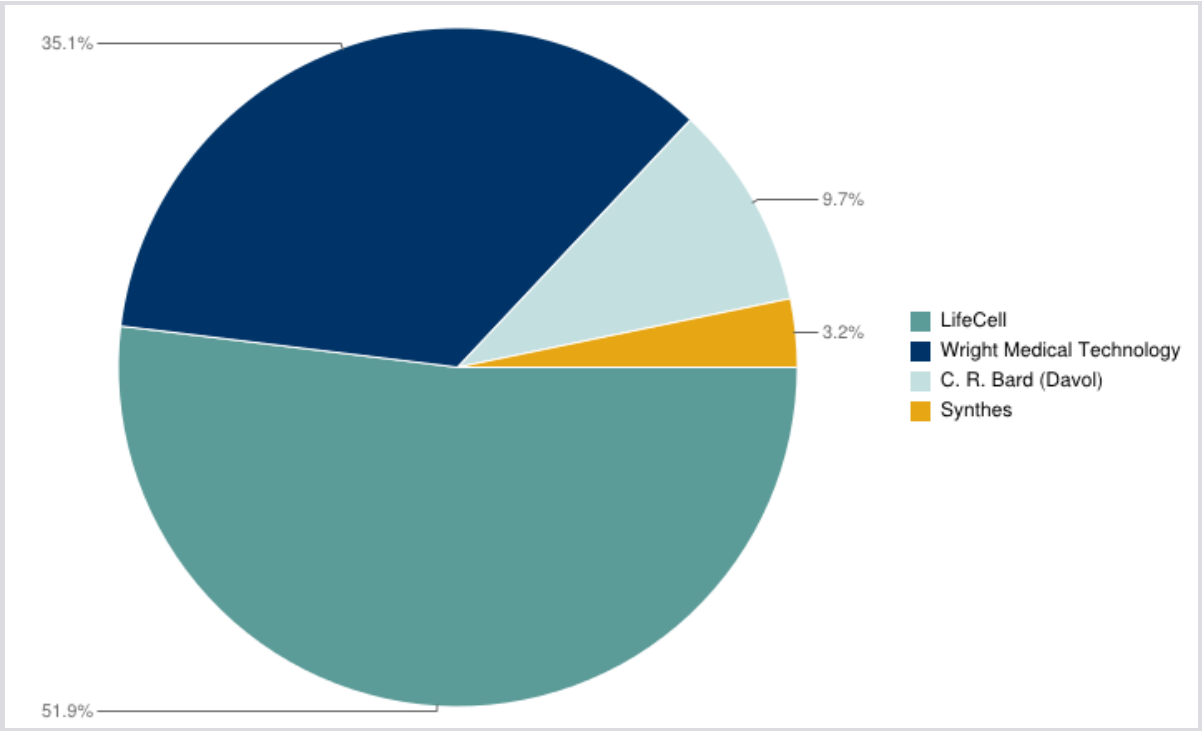
**Figure 15: Leading Competitors in the Imported Surgical Musculoskeletal and Soft Tissue Allograft Market, as a % of Total, Canada, 2012**




Notes: (1) Numbers reflect rounding. (2) Other includes Arteriocyte Medical Systems, Atrium Medical, Bacterin International, Biomet, Codman & Shurtleff, Community Tissue Services, DePuy, Harvest Technologies, J. K. Orthomedic, LifeLink Tissue Bank, LifeNet Health, pfm medical, Puget Sound Blood Center, RegenMed, Rocky Mountain Tissue Bank, Sorin Group, Synovis Life Technologies, Tissue Bank Manitoba, TissueNet, and Zimmer.

Source: Millennium Research Group

**Figure 16: Leading Competitors in the Imported Surgical ADM Market, as a % of Total, Canada, 2012**




Notes: (1) Numbers reflect rounding. (2) The imported reinforcement graft market comprises only Wright Medical Technology.

Source: Millennium Research Group

# APPENDIX: METHODOLOGY

## RESEARCH METHODOLOGY

This report uses a number of methodologies to gather and present data and analysis. At the outset, a large survey of secondary sources is conducted. These sources act as the basis for the primary research stage, which builds and enhances the quantitative and qualitative attributes of the early research. Secondary sources include

- government publications, such as documentation from securities commissions, health care and statistical agencies, and regulatory and patent authorities;
- procedural information from the Canadian Institute for Health Information and Régie de l'assurance maladie du Québec
- material provided by medical technology companies competing in the allograft and acellular dermal matrix (ADM) market, including annual reports, product brochures, and corporate profiles;
- internal databases and reports, including previous reports on similar or related topics; and
- general Internet searches, medical literature, and newspaper and magazine searches to identify various centers of specialization and articles that might provide leads for primary research.

The secondary research stage builds the foundation for the primary research. The primary research methodology has four steps:

**Step 1:** The first step involves an impartial scan of all the information gathered during the secondary research stage to determine its utility based on the specific requirements of this report. Each piece of information is either discarded or marked as high- or low-priority and then organized appropriately as determined by the structure and sectioning of the report.

**Step 2:** At this stage, early assumptions are formed as to the implications of the information for the various market segments. These assumptions are then used to determine hypotheses using both inductive and deductive approaches. On the quantitative front, these hypotheses result in full historical and projected market data sets (market sizes—unit sales, ASPs, and revenues—as well as market shares).

**Step 3:** At this stage, the research is in position for its most important primary phase—expert interviews. Throughout the secondary research phase, industry and medical experts are identified. These experts are then contacted by telephone and asked to participate in interviews on recent trends and developments in the industry. Interviews are either conducted at the time of the initial call or scheduled at the convenience of the expert. Interview questions are tailored to the expertise of each particular interviewee, although in most cases, the most important questions are asked of all experts. The questions are largely based on the assumptions and hypotheses developed in Step 2, which are then augmented, discarded, or adjusted based on the views and positions put forth. Attempts are made, whenever possible, to cross-check the

views of various experts against each other and to reach positions of consensus on issues and market numbers.

In addition, a sample of relevant physicians is also interviewed by telephone. Physicians are asked to comment on various issues and trends, both in their own practice and in the overall market. The responses provided are then used to strengthen or augment the assumptions and hypotheses developed during the primary research phase. For the purpose of this study, a total of 5 interviews with Canadian physicians were conducted. Each physician interview was approximately 30 minutes in length and consisted of speaking to 1 general orthopedic surgeon, 1 neurosurgeon, 1 spinal surgeon, and 2 orthopedic surgeons specializing in sports medicine.

**Step 4:** The final stage of primary research involves individual and group analysis by Millennium Research Group. All research results are assessed and cross-checked thoroughly to determine their validity, relevance, and weight. From this process, qualitative conclusions are reached and data points finalized.

# FORECAST METHODOLOGY

In addition to the research methodology outlined above, the following "bottom-up" methodology is used to develop forecast assumptions for the report.

A comprehensive breakdown of various allograft and ADM procedures and unit sales is prepared using data from several sources, including professional associations, government statistics, and private research/media sources. Industry experts and practitioners are consulted to ensure accuracy and verify observed trends. As a cross-check, total industry revenues available through annual reports and other sources are compared against modeled industry revenues.

Using the best estimates of industry experts, practitioners, private research/media sources, and in-house experts, year-by-year growth rates and ASPs are applied individually to each subcategory to derive forecasts. These estimates are cross-checked by industry experts (marketing managers, product managers, company executives, etc.) as well as physicians and further refined.

Overall findings are compared against market and procedure forecasts published by other sources to ensure reasonable estimates.

# CANADIAN TISSUE BANK SUPPLY CALCULATION METHODOLOGY

As of December 2012, the most up-to-date available data on the domestic Canadian tissue bank supply for all of Canada, with the exception of Quebec, was from 2008. Consequently, Millennium Research Group utilized a variety of primary and secondary resources to extrapolate the domestic Canadian tissue bank supply to 2012. Below is a general outline of the inputs that went into this extrapolation process:

- Millennium Research Group's analysis of primary and secondary resources, including CIHI and RAMQ/MED-ECHO databases, resulted in understanding the total volume of procedures that utilized musculoskeletal allografts and ADMs in Canada.

» Through the evaluation of primary and secondary resources, including industry- and physician-based primary research and analysis of key competitor revenues, Millennium Research Group was able to identify total imported volumes of musculoskeletal allografts and ADMs in Canada.

» With an understanding of the average volume of material used per procedure and the volume of imported musculoskeletal allograft and ADMs, Millennium Research Group was able to identify the volume of domestic Canadian tissue bank supply.

» Utilizing qualitative and quantitative growth rate benchmarks of each product type (i.e., proprietary allografts, nonproprietary allografts, DBMs, and ADMs), Millennium Research Group was able to calculate a realistic growth rate for the domestic Canadian tissue bank supply from 2008 to 2012.

» Growth rates for the domestic and imported tissue supply from 2008 to 2012 were discussed and validated during industry-based primary research.

» The change in percentage of domestic tissue supply versus imported tissue volumes from 2008 to 2012 were also validated through primary and secondary resources.

» For Quebec, the Héma-Québec Tissue Bank Distribution booklet provided data up to March 2012. Because the fiscal year for this database is from April to the end of March, the data had to be adjusted to an annual volume of January to December for each calendar year. Additionally, the human tissue categories from the Héma-Québec Tissue Distribution booklet were redistributed to the categories that were being utilized for the rest of Canada from the domestic Canadian tissue bank supply database. Once these two steps were completed, the information for Quebec was incorporated into the rest of Canada to calculate the overall domestic Canadian tissue bank supply for 2012.

# APPENDIX: ACRONYMS AND INITIALISMS

**Table 153: Acronyms and Initialisms**

| Acronym/Initialism | Definition |
|---|---|
| ACL | Anterior Cruciate Ligament |
| ADM | Acellular Dermal Matrix |
| ASP | Average Selling Price |
| BGS | Bone Graft Substitute(s) |
| BMA | Bone Marrow Aspirate |
| BMAC | Bone Marrow Aspirate Concentrate |
| BMP | Bone Morphogenetic Protein |
| BTB | Bone-Patellar Tendon-Bone |
| CAD | Canadian Dollar |
| CAGR | Compound Annual Growth Rate |
| CIA | Central Intelligence Agency |
| CMF | Craniomaxillofacial |
| CSF | Cerebrospinal Fluid |
| DBM | Demineralized Bone Matrix |
| DDD | Degenerative Disc Disease |
| GDP | Gross Domestic Product |
| GPO | Group Purchasing Organization |
| HIV | Human Immunodeficiency Virus |
| IBD | Interbody Device |
| ISO | International Organization for Standardization |
| LCL | Lateral Collateral Ligament |
| MCL | Medial Collateral Ligament |
| MDEL | Medical Device Establishment License |
| MSC | Mesenchymal Stem Cell |
| MTF | Musculoskeletal Transplant Foundation |
| OP-1 | Osteogenic Protein-1 |
| PCL | Posterior Cruciate Ligament |
| PEEK | Polyetheretherketone |
| PRP | Platelet-Rich Plasma |
| TCP | Tricalcium Phosphate |
| TGF | Transforming Growth Factor |
| TMJ | Temporomandibular Joint |
| USD | US Dollar |
| WHO | World Health Organization |
| Source: Millennium Research Group | |

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